OIPE IAP55 APR 25 2006 PATENT & TRADEMARK OFFICE

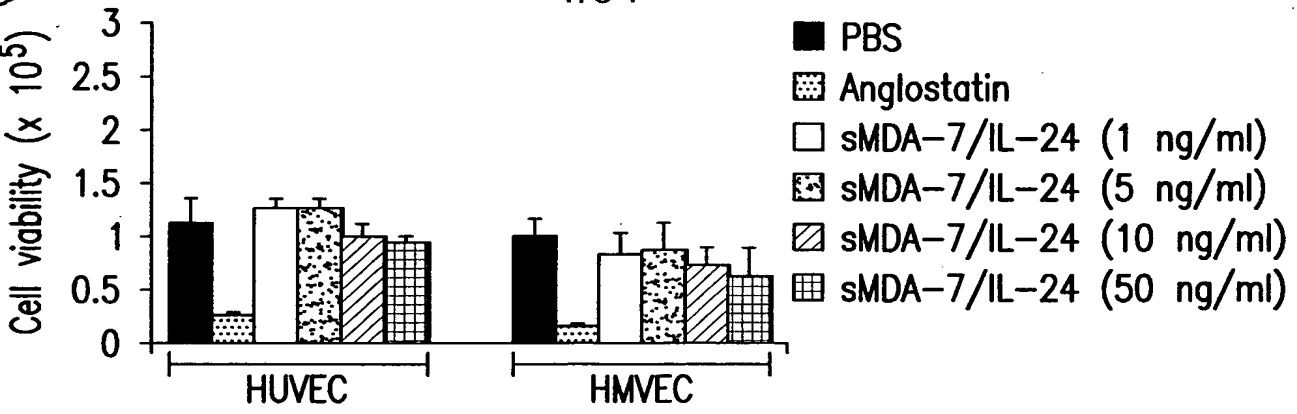


FIG.1A

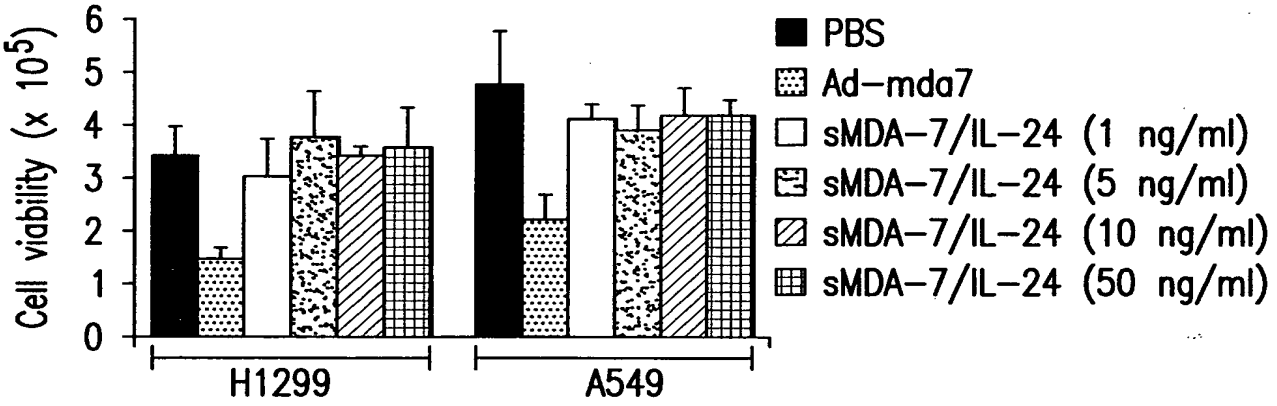


FIG.1B

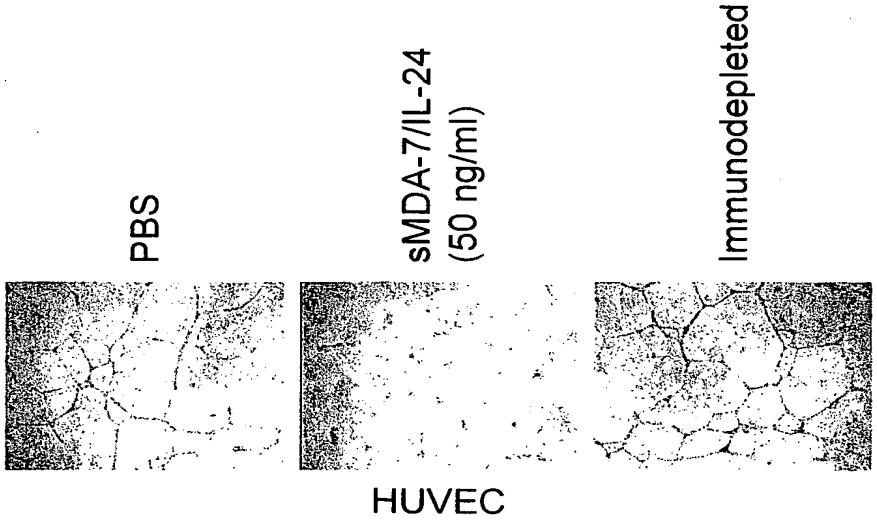


FIG.1C

BEST AVAILABLE COPY

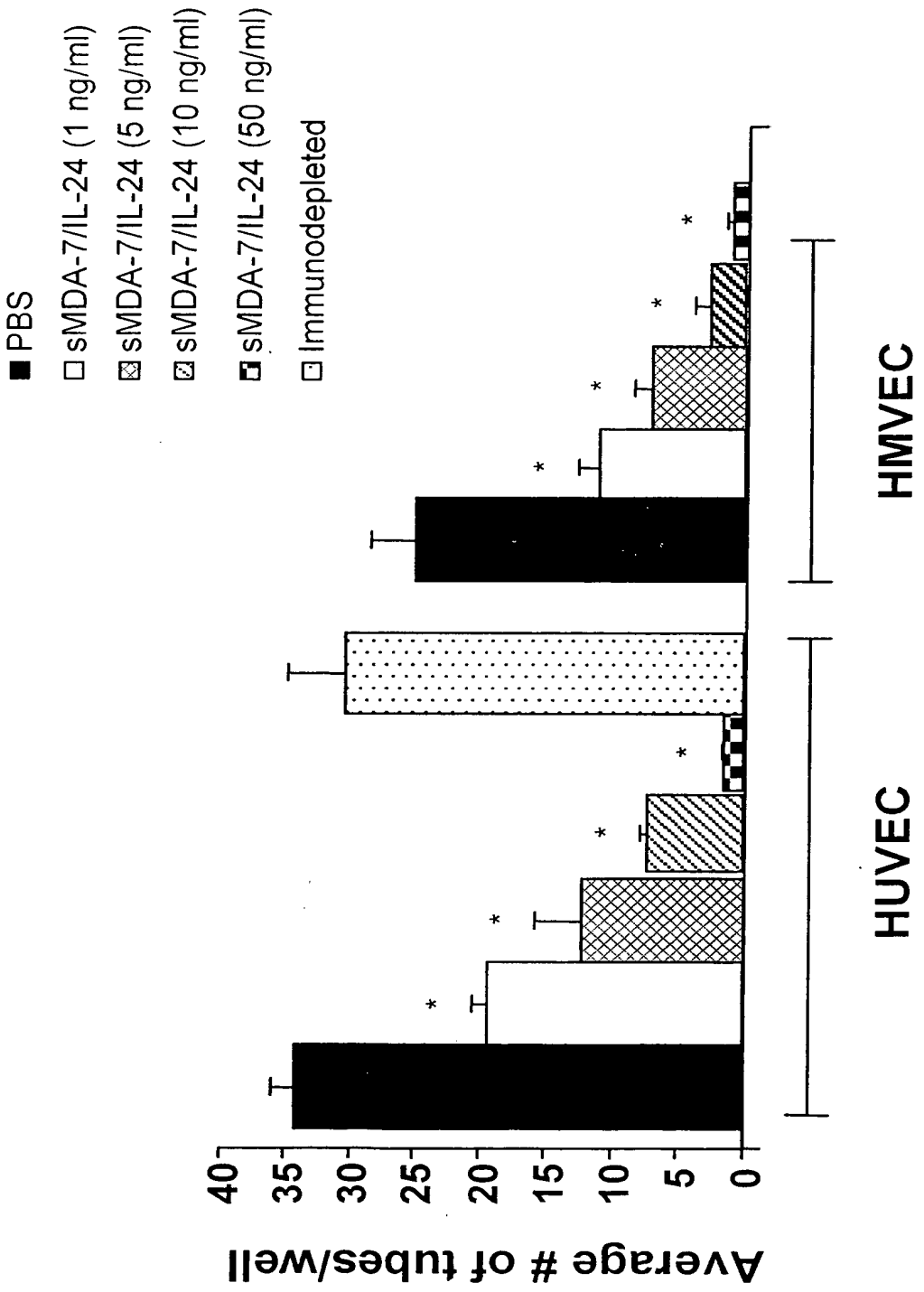

PBS
sMDA-7/IL-24 (1 ng/ml)
sMDA-7/IL-24 (5 ng/ml)
sMDA-7/IL-24 (10 ng/ml)
sMDA-7/IL-24 (50 ng/ml)
Immunodepleted
Average # of tubes/well
0
5
10
15
20
25
30
35
40
HUVEC
HMVEC

FIG. 1D

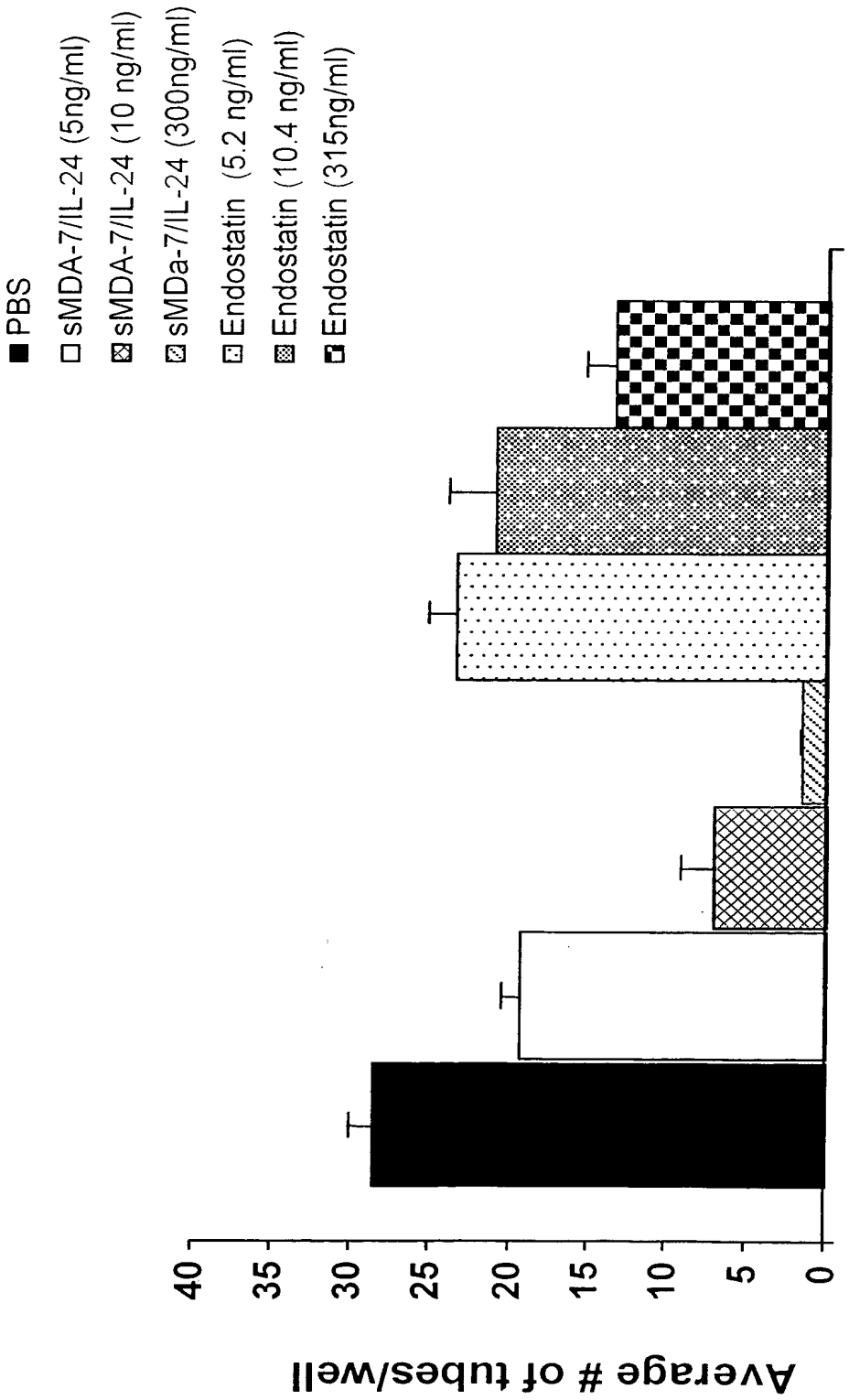

PBS
sMDA-7/IL-24 (5ng/ml)
sMDA-7/IL-24 (10 ng/ml)
sMDa-7/IL-24 (300ng/ml)
Endostatin (5.2 ng/ml)
Endostatin (10.4 ng/ml)
Endostatin (315ng/ml)
Average # of tubes/well
0
5
10
15
20
25
30
35
40
HUVEC

FIG.2

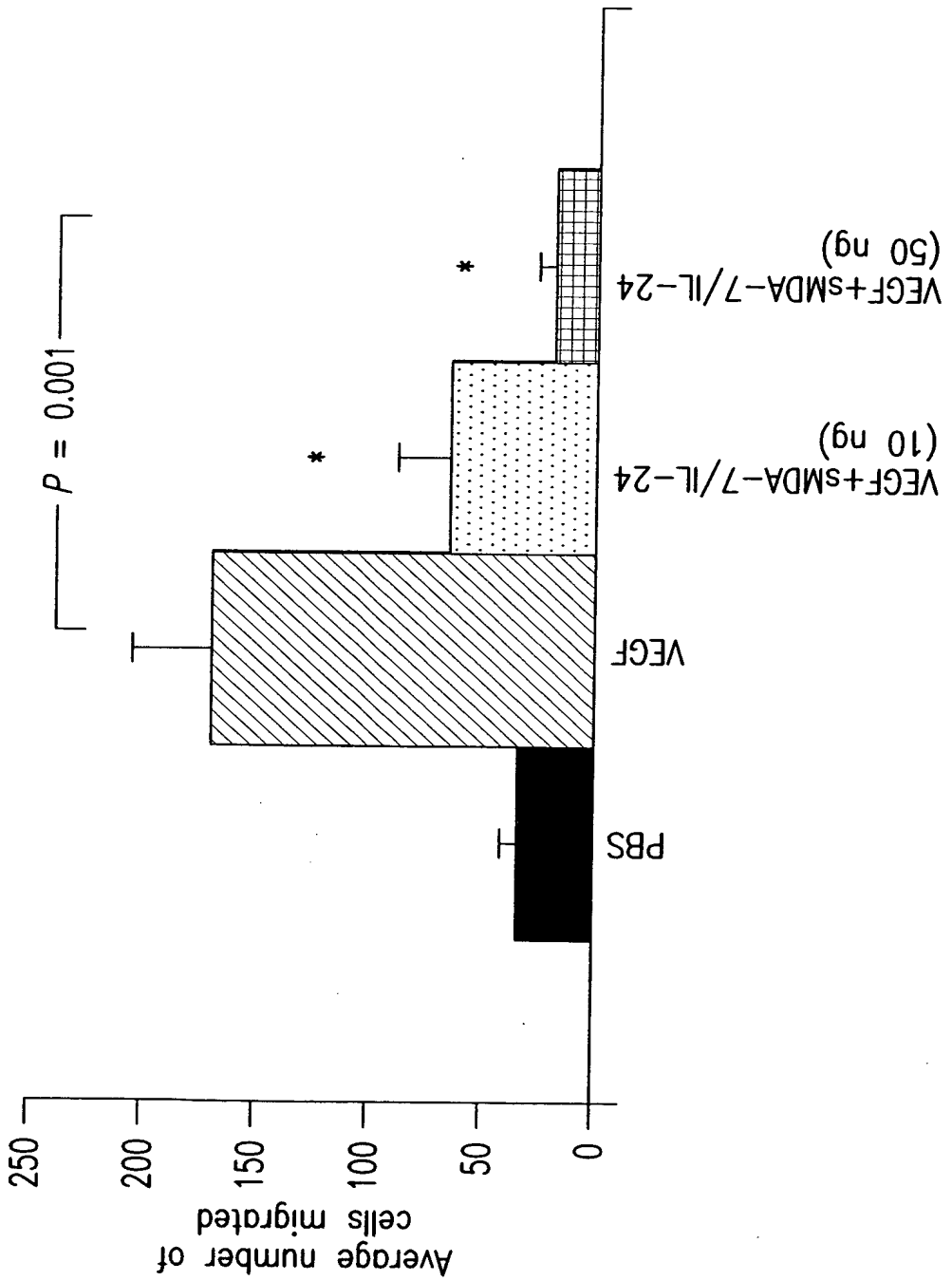

Average number of cells migrated
250
200
150
100
50
0
PBS
VEGF
VEGF+sMDA-7/IL-24 (10 ng)
VEGF+sMDA-7/IL-24 (50 ng)
*
*
P = 0.001

FIG.3

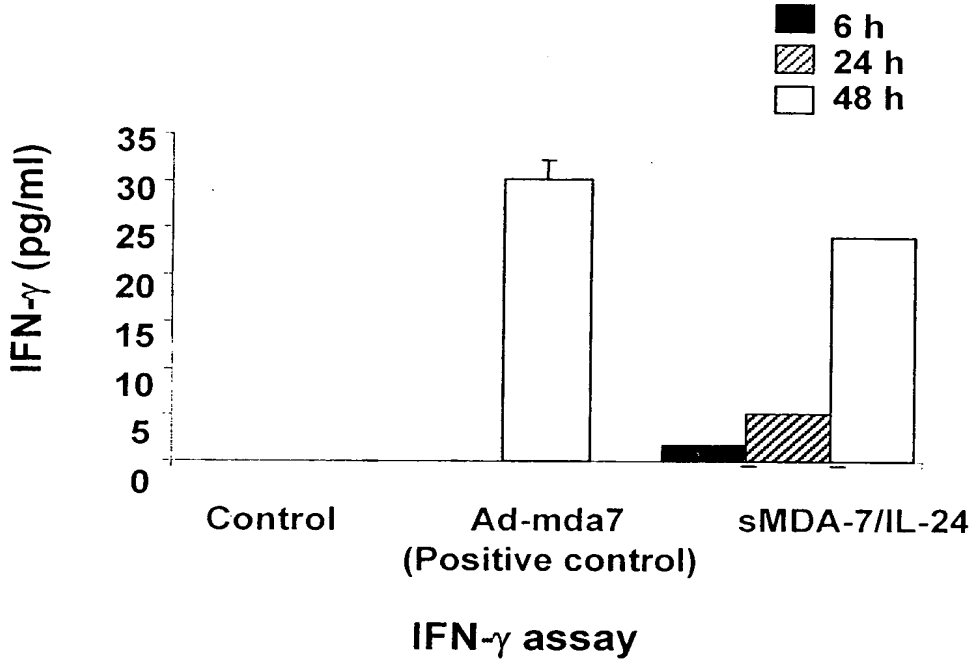

6 h
24 h
48 h
IFN-γ (pg/ml)
35
30
25
20
15
10
5
0
Control
Ad-mda7
(Positive control)
sMDA-7/IL-24
IFN-γ assay

FIG.4A

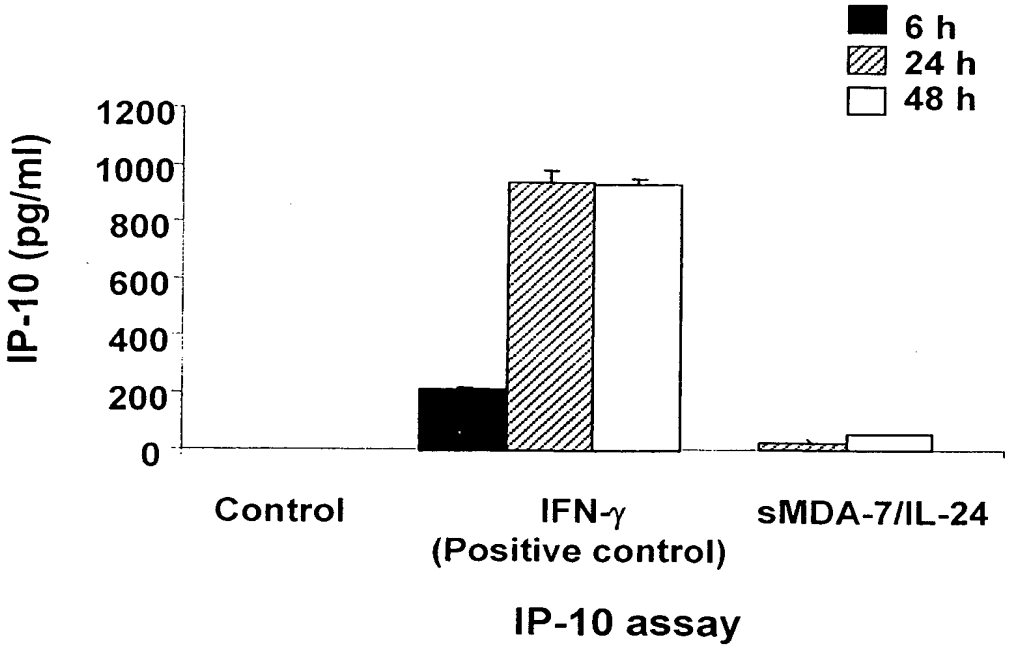

6 h
24 h
48 h
IP-10 (pg/ml)
1200
1000
800
600
400
200
0
Control
IFN-γ
(Positive control)
sMDA-7/IL-24
IP-10 assay

FIG.4B

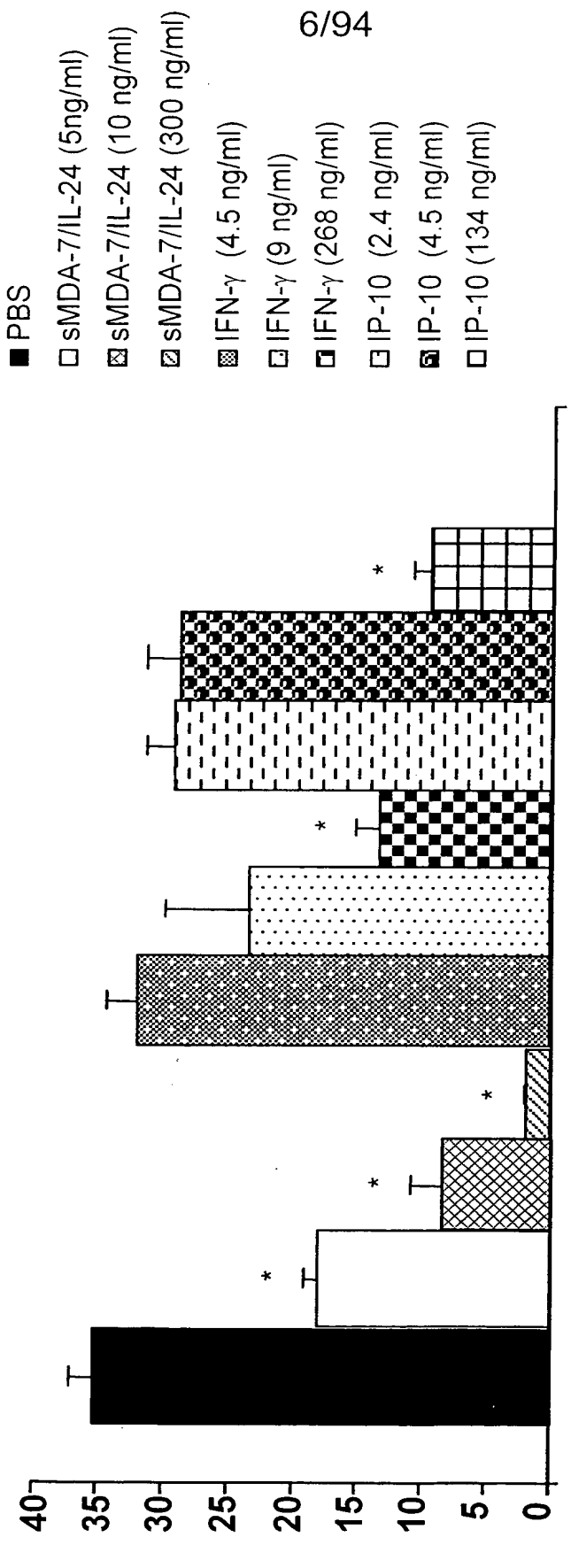

PBS
sMDA-7/IL-24 (5ng/ml)
sMDA-7/IL-24 (10 ng/ml)
sMDA-7/IL-24 (300 ng/ml)
IFN-γ (4.5 ng/ml)
IFN-γ (9 ng/ml)
IFN-γ (268 ng/ml)
IP-10 (2.4 ng/ml)
IP-10 (4.5 ng/ml)
IP-10 (134 ng/ml)
Average # of tubes/well
0
5
10
15
20
25
30
35
40
*
HUVEC

FIG.4C

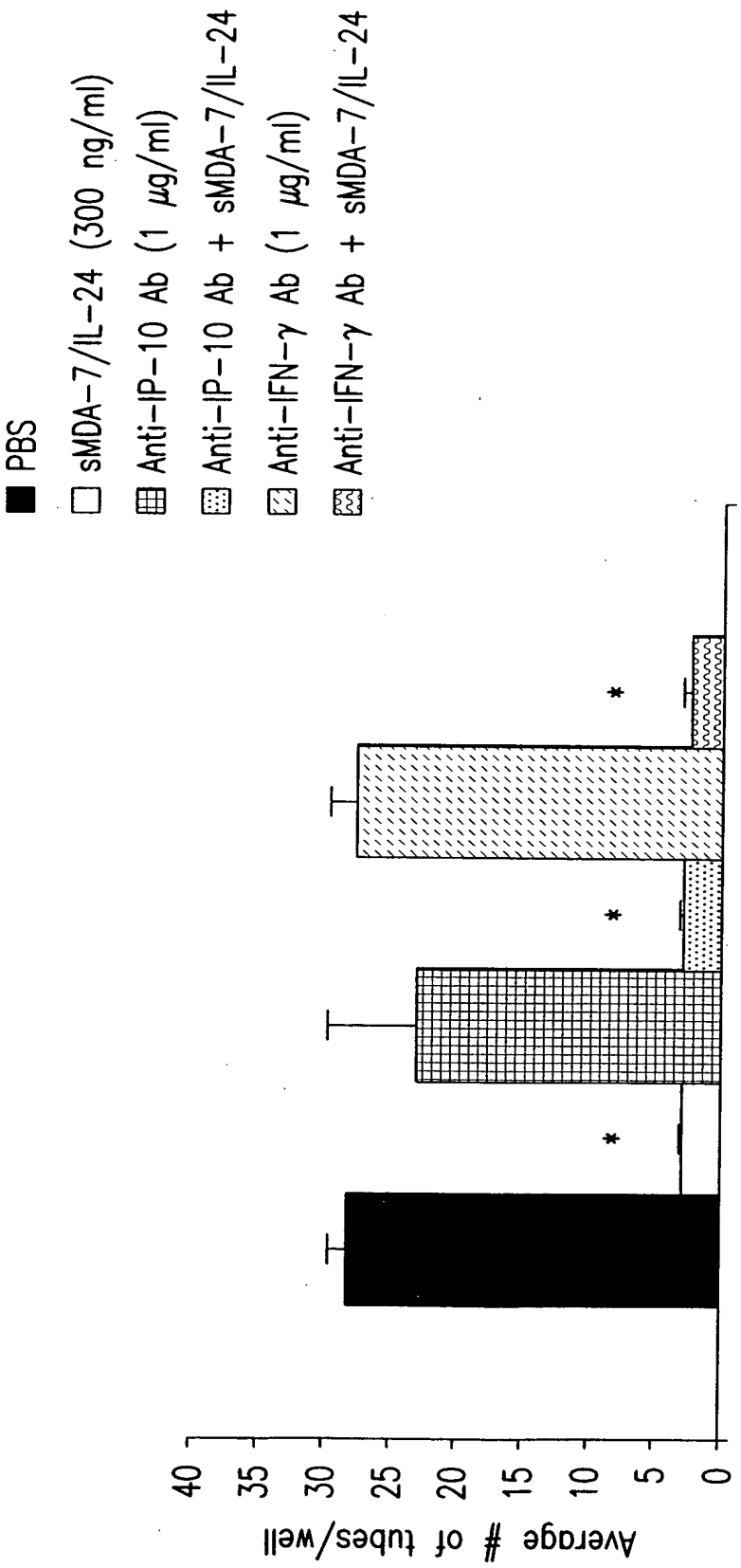

PBS
sMDA-7/IL-24 (300 ng/ml)
Anti-IP-10 Ab (1 μg/ml)
Anti-IP-10 Ab + sMDA-7/IL-24
Anti-IFN-γ Ab (1 μg/ml)
Anti-IFN-γ Ab + sMDA-7/IL-24
Average # of tubes/well
0
5
10
15
20
25
30
35
40
*
*
*
HUVEC

FIG.4D

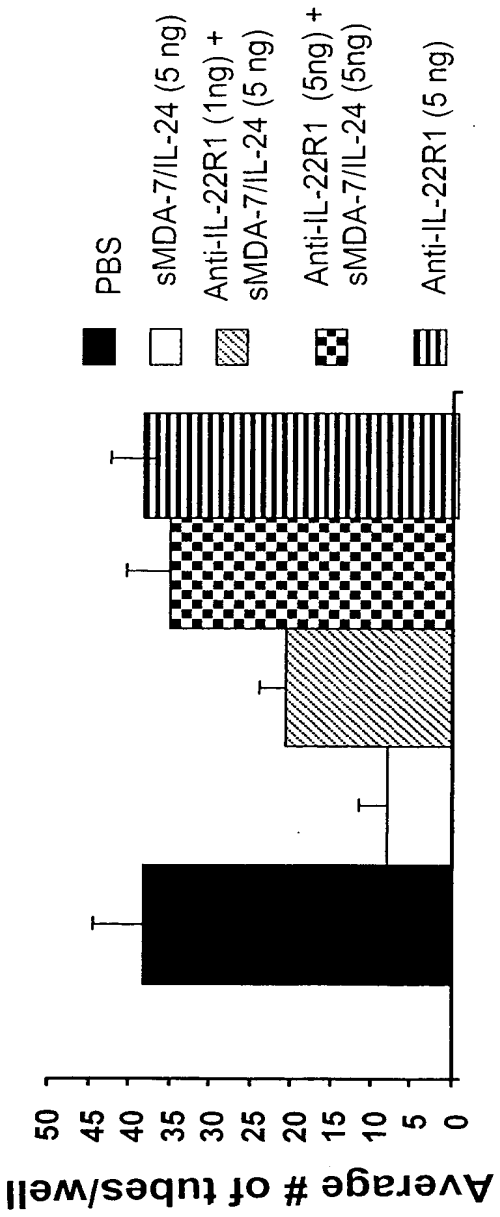

PBS
sMDA-7/IL-24 (5 ng)
Anti-IL-22R1 (1ng) + sMDA-7/IL-24 (5 ng)
Anti-IL-22R1 (5ng) + sMDA-7/IL-24 (5ng)
Anti-IL-22R1 (5 ng)
Average # of tubes/well
0
5
10
15
20
25
30
35
40
45
50

FIG.5A

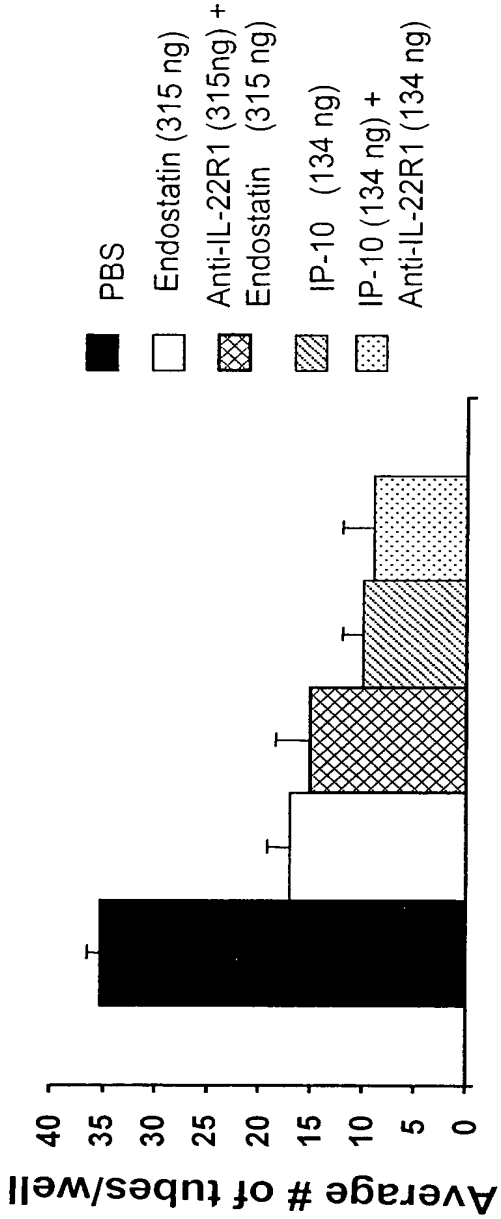

PBS
Endostatin (315 ng)
Anti-IL-22R1 (315ng) + Endostatin (315 ng)
IP-10 (134 ng)
IP-10 (134 ng) + Anti-IL-22R1 (134 ng)
Average # of tubes/well
0
5
10
15
20
25
30
35
40

FIG.5B

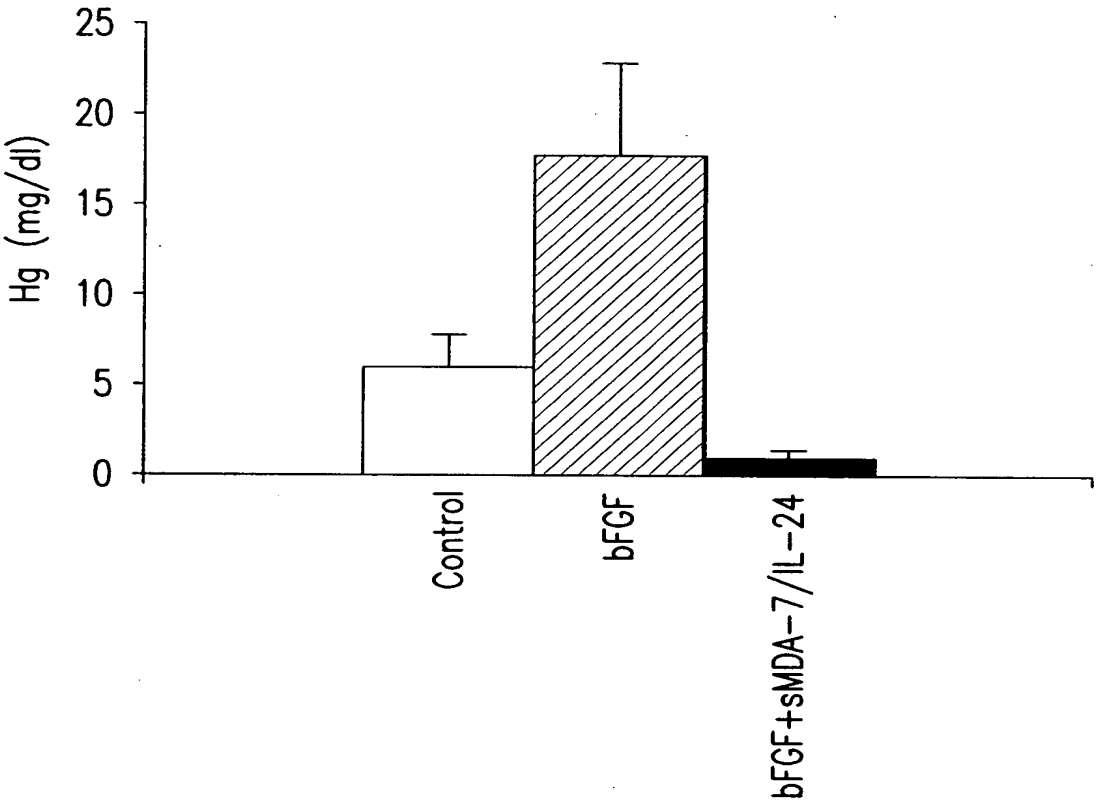


FIG.6A

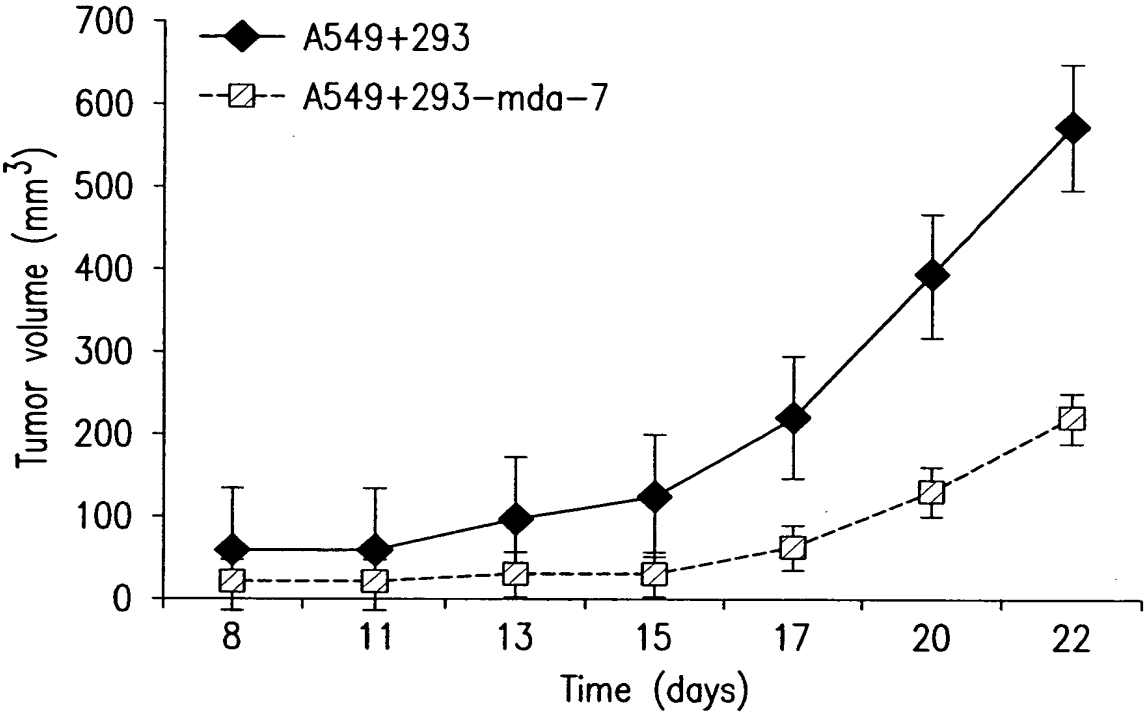

700
600
500
400
300
200
100
0
Tumor volume (mm3)
A549+293
A549+293-mda-7
8
11
13
15
17
20
22
Time (days)

FIG.6B

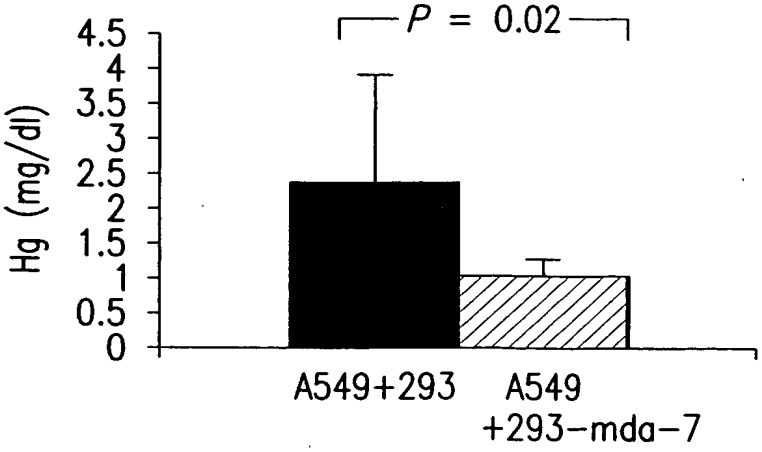

P = 0.02
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
Hg (mg/dl)
A549+293
A549 +293-mda-7

FIG.6C

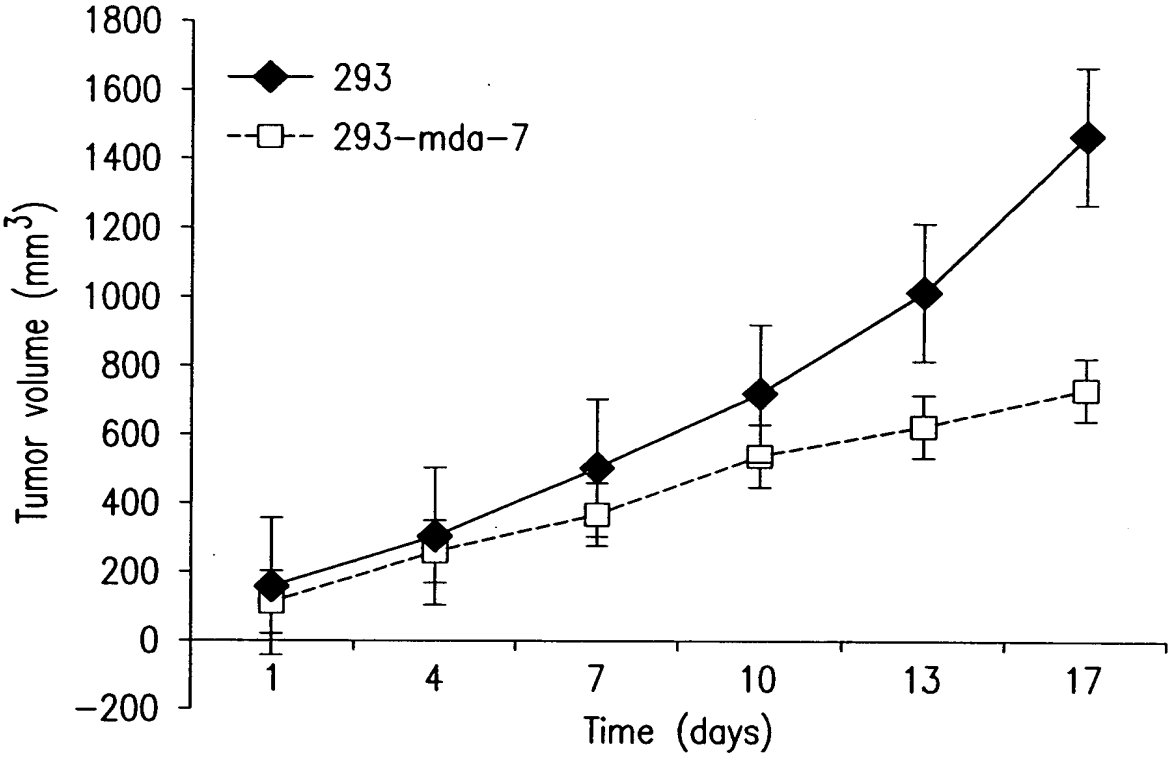

1800
1600
1400
1200
1000
800
600
400
200
0
−200
Tumor volume (mm3)
293
293−mda−7
1
4
7
10
13
17
Time (days)

FIG.6D

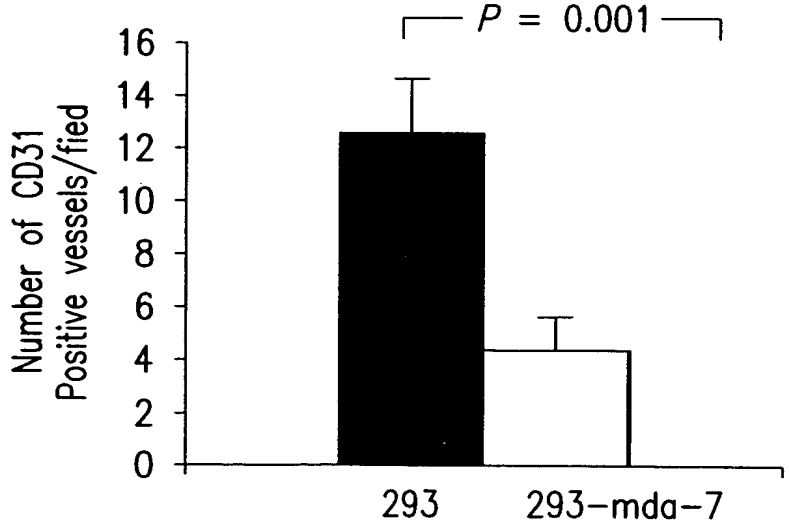

P = 0.001
16
14
12
10
8
6
4
2
0
Number of CD31
Positive vessels/fied
293
293−mda−7

FIG.6E

Study design

Cohort #	# of patients	Viral dose (particles)	biopsy time (post inj.)
1	1	$2x10^{10}$	24 hrs
2	1	$2x10^{11}$	24 hrs
3	3	$2x10^{12}$	24 hrs
4	3	$2x10^{12}$	48 hrs
5	3	$2x10^{12}$	72/96 hrs
6	3	$2x10^{12}$ (divided doses)	48 hrs
7	5	$2x10^{12}$	Core bx @30 days
8	5	$2x10^{12}$ (2x/wk x 3 wks)	Core bx @ 30 days

FIG.7

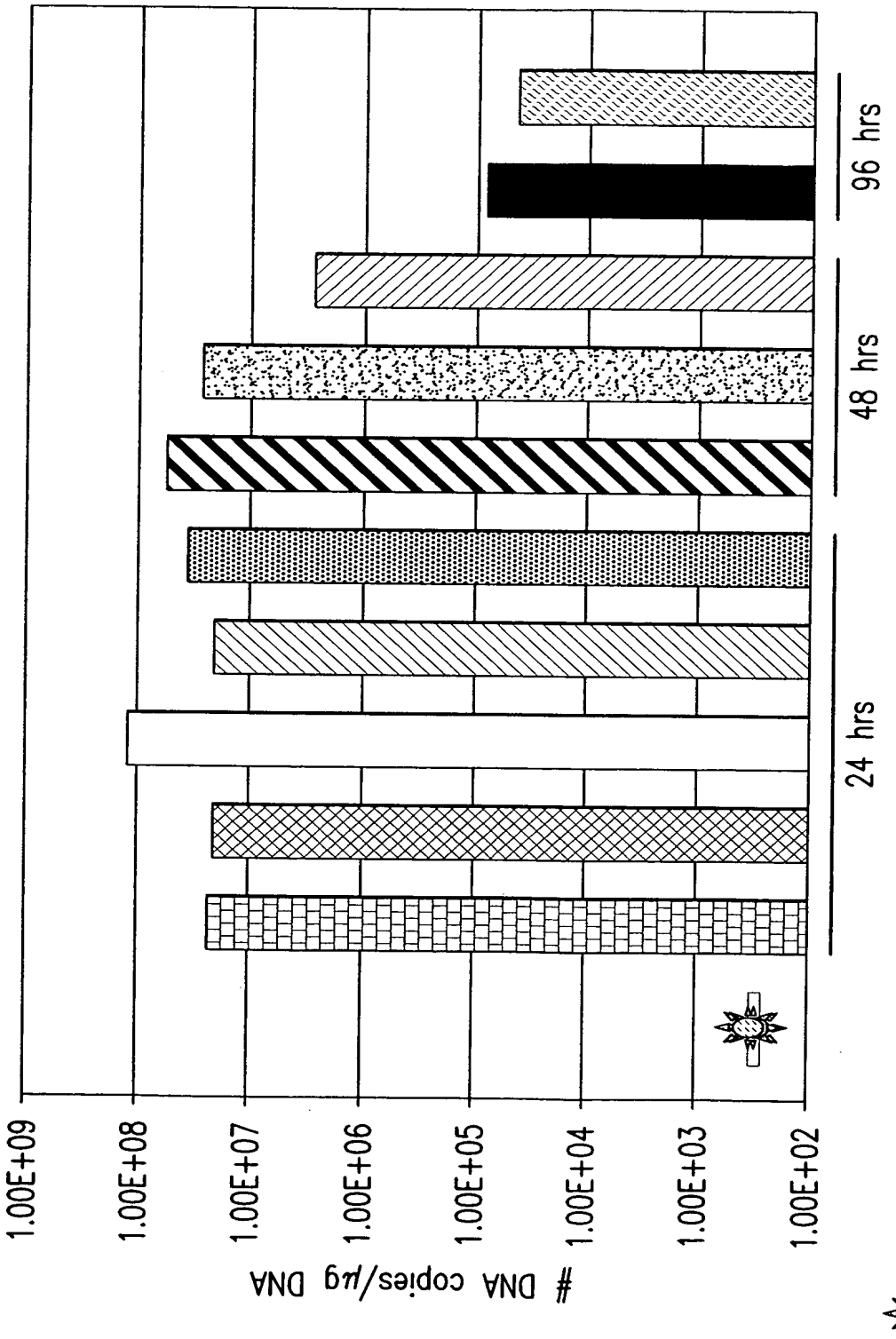

DNA copies/μg DNA
1.00E+09
1.00E+08
1.00E+07
1.00E+06
1.00E+05
1.00E+04
1.00E+03
1.00E+02
24 hrs
48 hrs
96 hrs
: Average pre-treat signal is 4.4E+02, n=8

FIG.8

(Pre-treat MDA-7 IHC – all negative)

Pt	Time (hr)	MDA-7 ctr	MDA-7 periph	TUNEL ctr	TUNEL periph
1	24	20%	0%	20%	0%
2	24	30%	5%	70%	10%
3	24	75%	40%	50%	30%
4	24	35%	5%	n.d.	n.d.
5	24	50%	25%	25%	17%
6	48	>60%	20%	40%	17%
7	48	60%	5%	70%	10%
8	48	20%	0%	5%	0%
9	96	50%	25%	80%	25%
10	96	90%	0%	35%	0%

MDA-7/TUNEL correlation $p<0.01$

FIG.9

Replacement Sheet

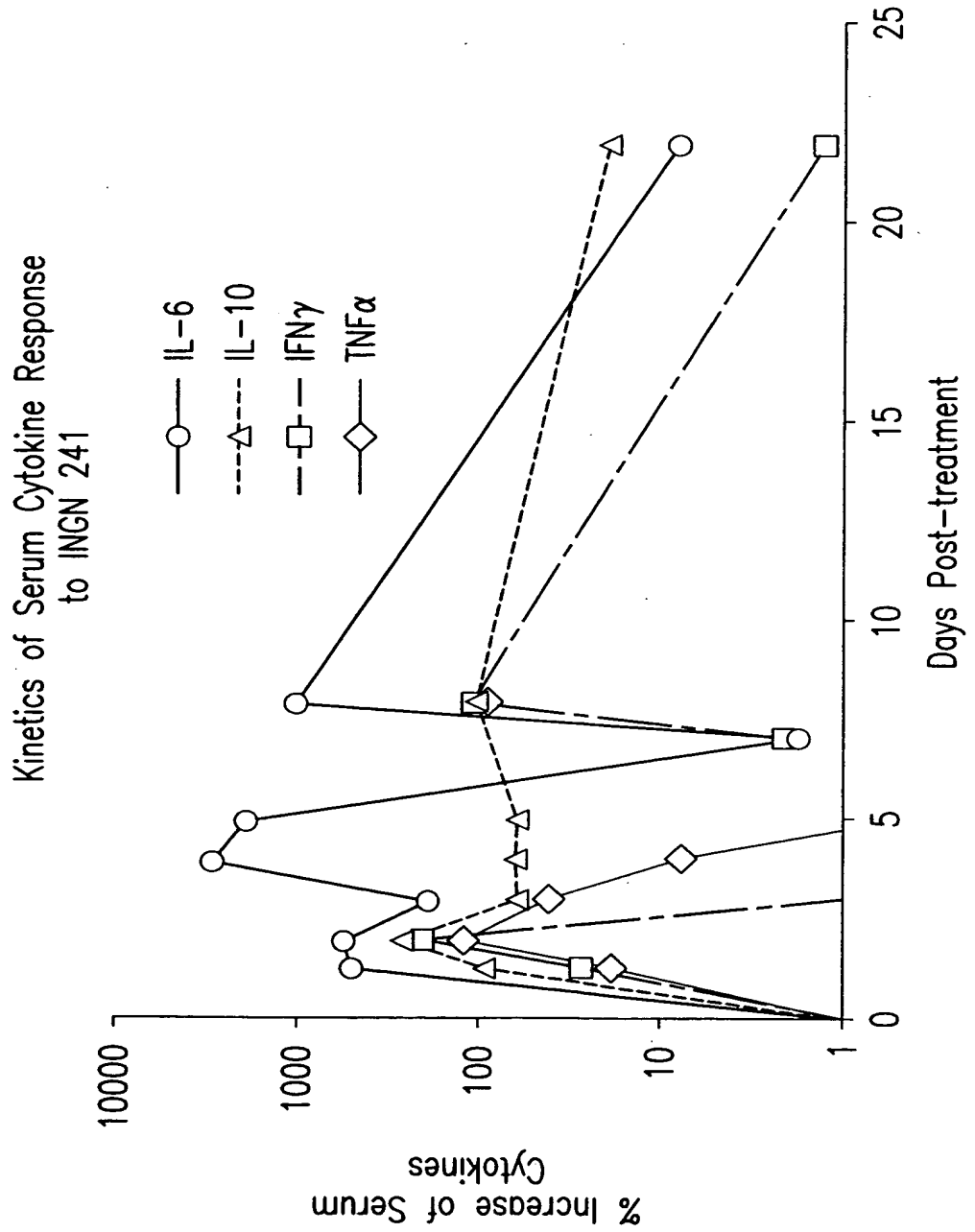

Kinetics of Serum Cytokine Response
to INGN 241
IL-6
IL-10
IFNγ
TNFα
% Increase of Serum
Cytokines
10000
1000
100
10
1
0
5
10
15
20
25
Days Post-treatment

FIG.10

Serum Cytokine Response to
Intratumoral INGN 241 Treatment.

Cohort (dose)	No. pts tested	No. positive (mean % peak increase) IL-6	IL-10	IFNγ	TNFα	GM-CSF
1 ($2x10^{10}$)	1	1 (298%)	1 (291%)	1 (>1,000%)	0	1 (150%)
2 ($2x10^{11}$)	1	1 (143%)	1 (599%)	1 (281%)	1 (864%)	0
3 ($2x10^{12}$)	3	1 (>1,000%)	1 (134%)	1 (317%)	2 (345%)	1 (100%)
4 ($2x10^{12}$)	3	3 (>1,000%)	3 (221%)	1 (173%)	2 (71%)	1 (120%)
5 ($2x10^{12}$)	3	3 (640%)	3 (400%)	1 (317%)	2 (156%)	0
7 ($2x10^{12}$)	7	5 (604%)	6 (387%)	3 (860%)	3 (255%)	0
Total	18	14	15	8	10	3

FIG.11

Replacement Sheet

Level of Increased CD8 + T cell Frequency in Pts who Received Intratumoral INGN 241.

Cohort (dose)	No. pts tested	No. with increased CD8 + T cells	Mean % CD3 + CD8 + T cells[1] Pre-treatment	Post-treatment @	Day Post-treat.
1 ($2x10^{10}$)	1	0	29%	27%	
2 ($2x10^{11}$)	1	1	32%	44%	Day 15
3 ($2x10^{12}$)	3	3	33%	59%	Day 15
4 ($2x10^{12}$)	3	1	35%	44%	Day 30
5 ($2x10^{12}$)	3	1	22%	29%	Day 15
7 ($2x10^{12}$)	7	2	30%	40%	Days 15-30
Total	18	8	31%	44%	Day 15

FIG.12

Replacement Sheet

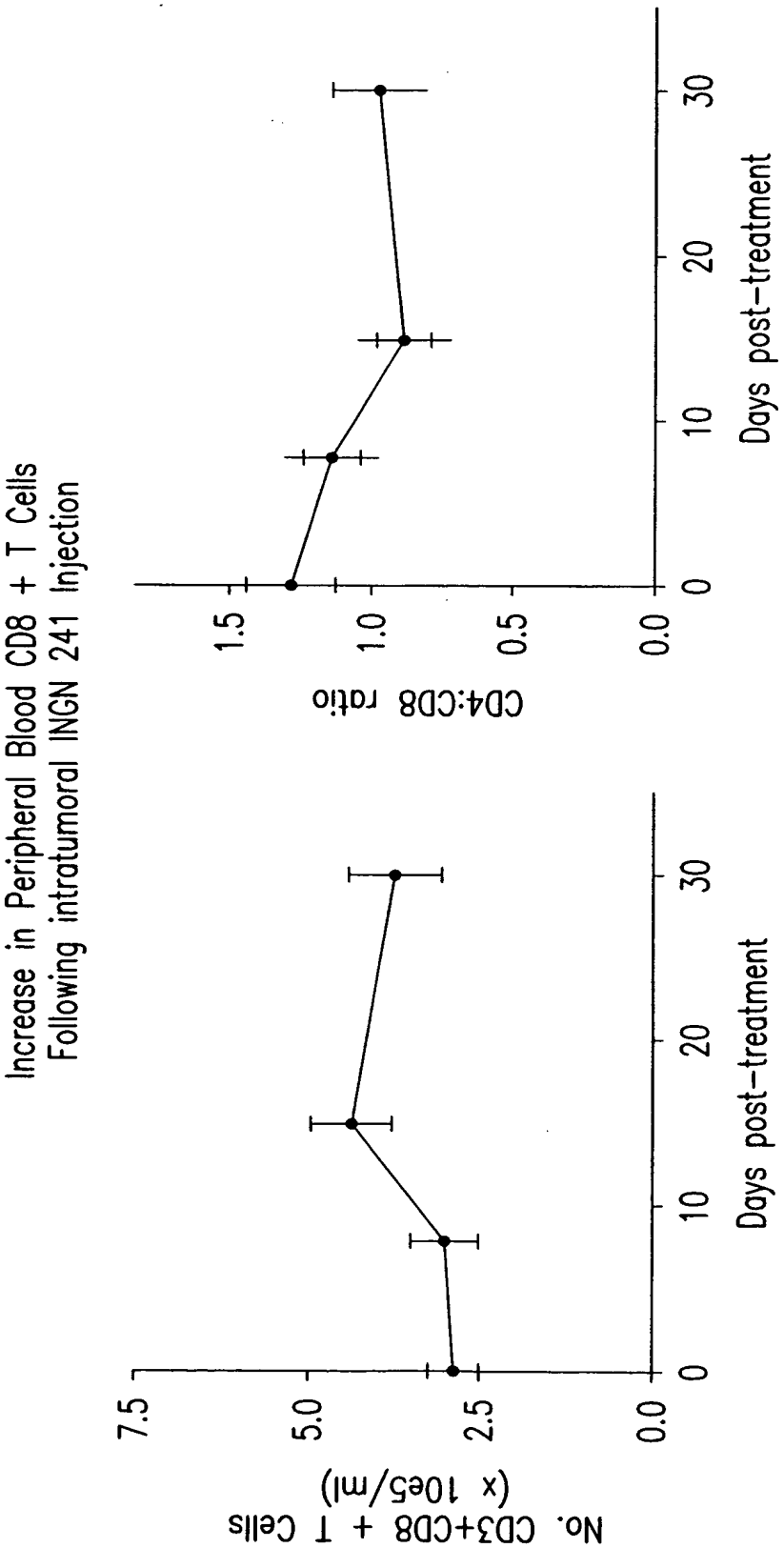

Increase in Peripheral Blood CD8 + T Cells
Following intratumoral INGN 241 Injection
No. CD3+CD8 + T Cells
(x 10e5/ml)
7.5
5.0
2.5
0.0
0
10
20
30
Days post-treatment
CD4:CD8 ratio
1.5
1.0
0.5
0.0
0
10
20
30
Days post-treatment

FIG. 13

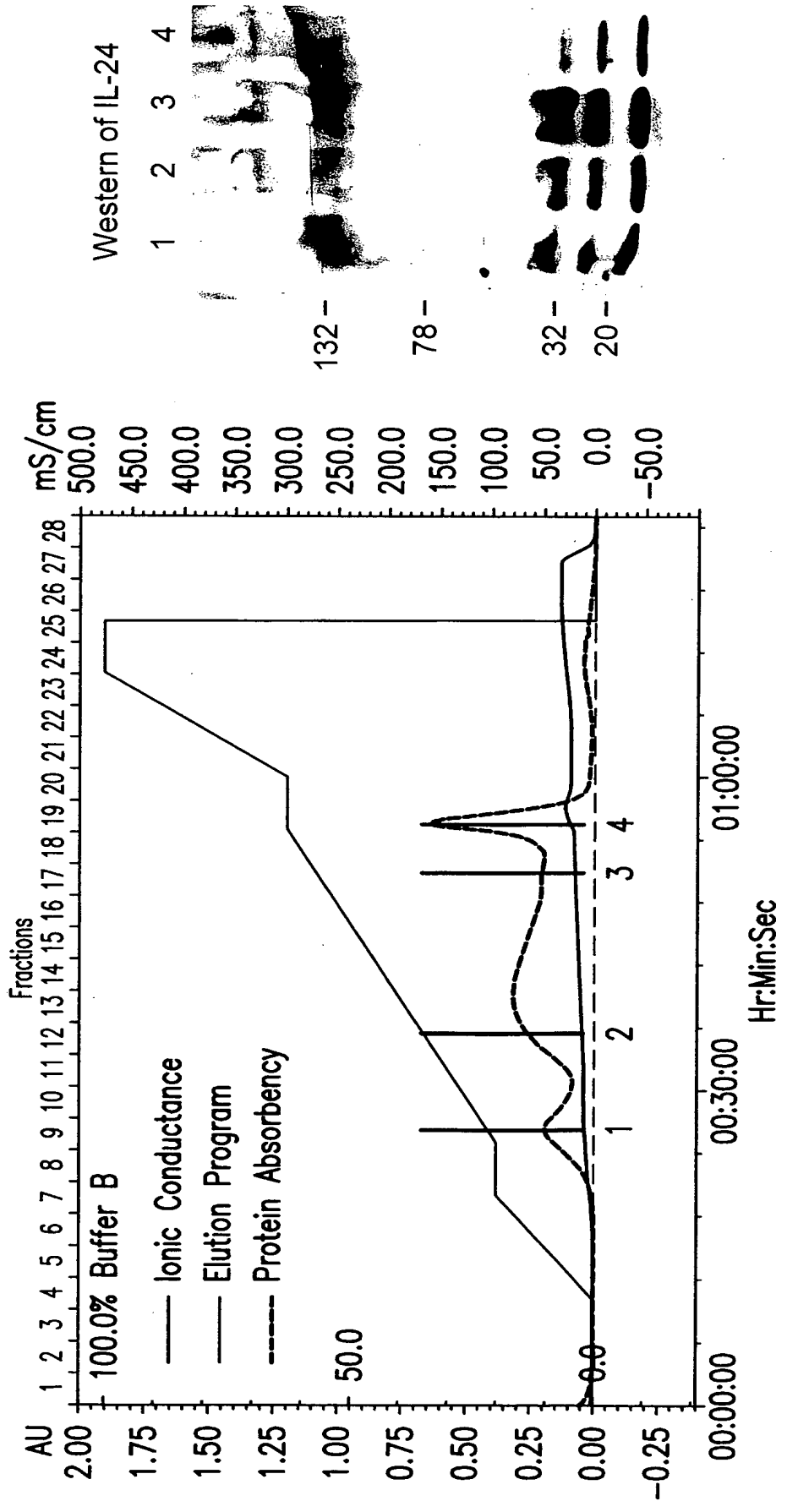

Western of IL-24
1 2 3 4
132
78
32
20
mS/cm
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
-50.0
Fractions
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
100.0% Buffer B
50.0
0.0
Ionic Conductance
Elution Program
Protein Absorbency
AU
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
-0.25
00:00:00
00:30:00
01:00:00
Hr:Min:Sec
1
2
3
4

FIG.14

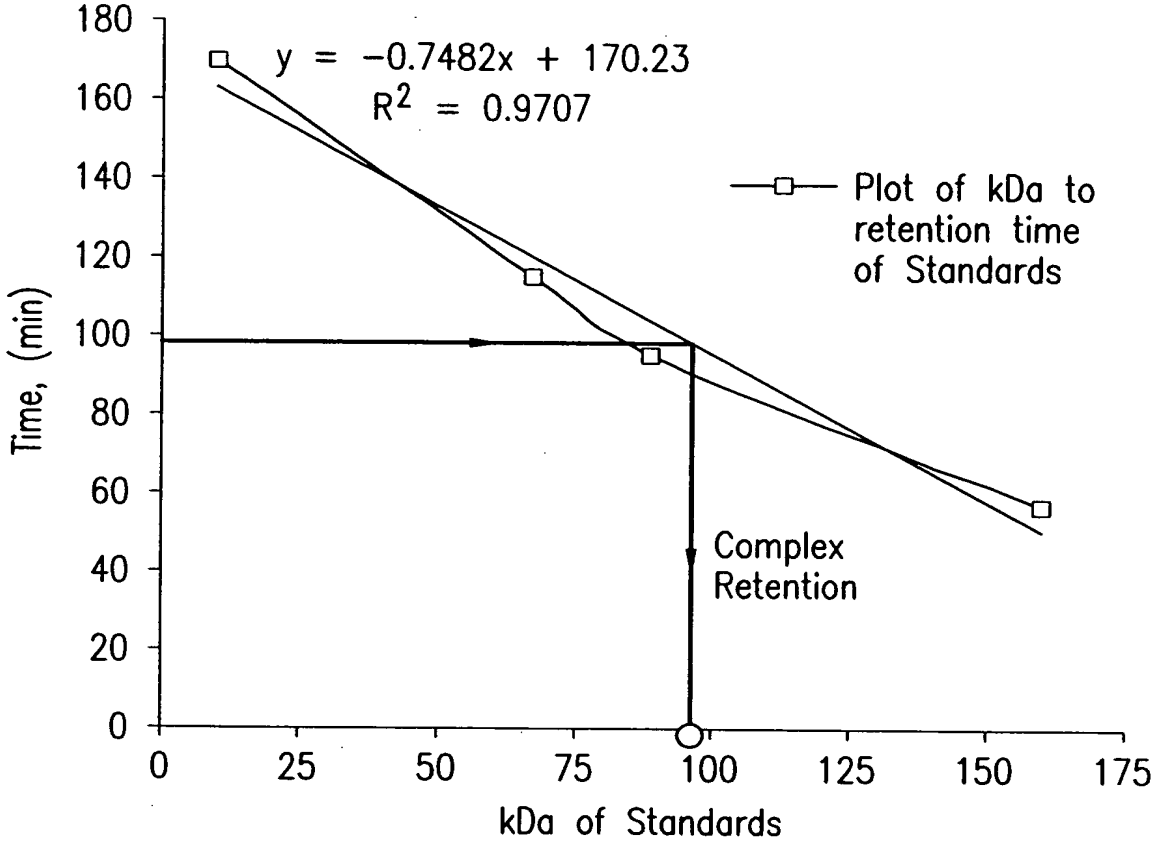

y = −0.7482x + 170.23
R2 = 0.9707
Plot of kDa to retention time of Standards
Complex Retention
Time, (min)
kDa of Standards
180
160
140
120
100
80
60
40
20
0
0
25
50
75
100
125
150
175

FIG.15

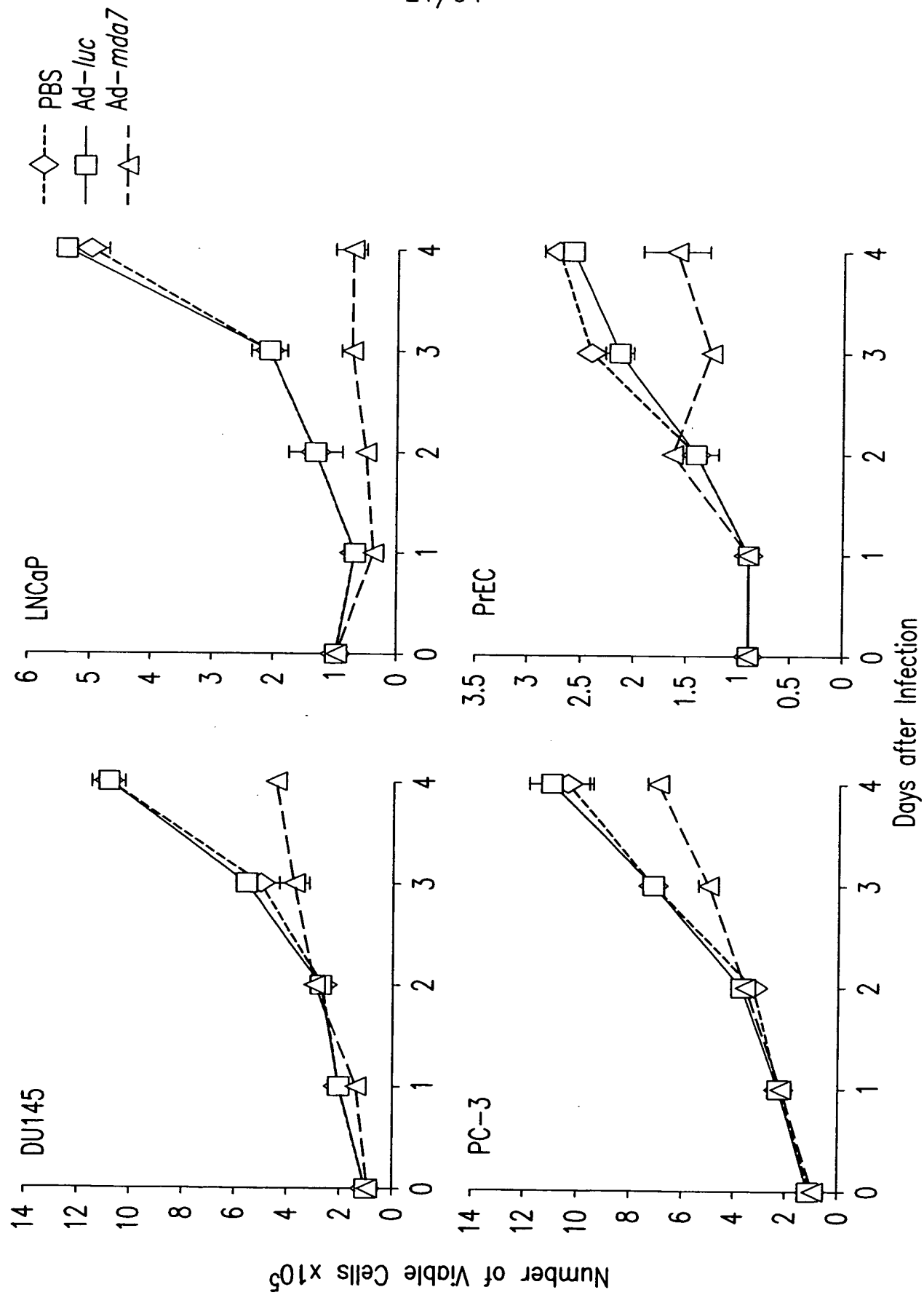

PBS
Ad-luc
Ad-mda7
LNCaP
PrEC
DU145
PC-3
Number of Viable Cells x10^5
Days after Infection

FIG.16

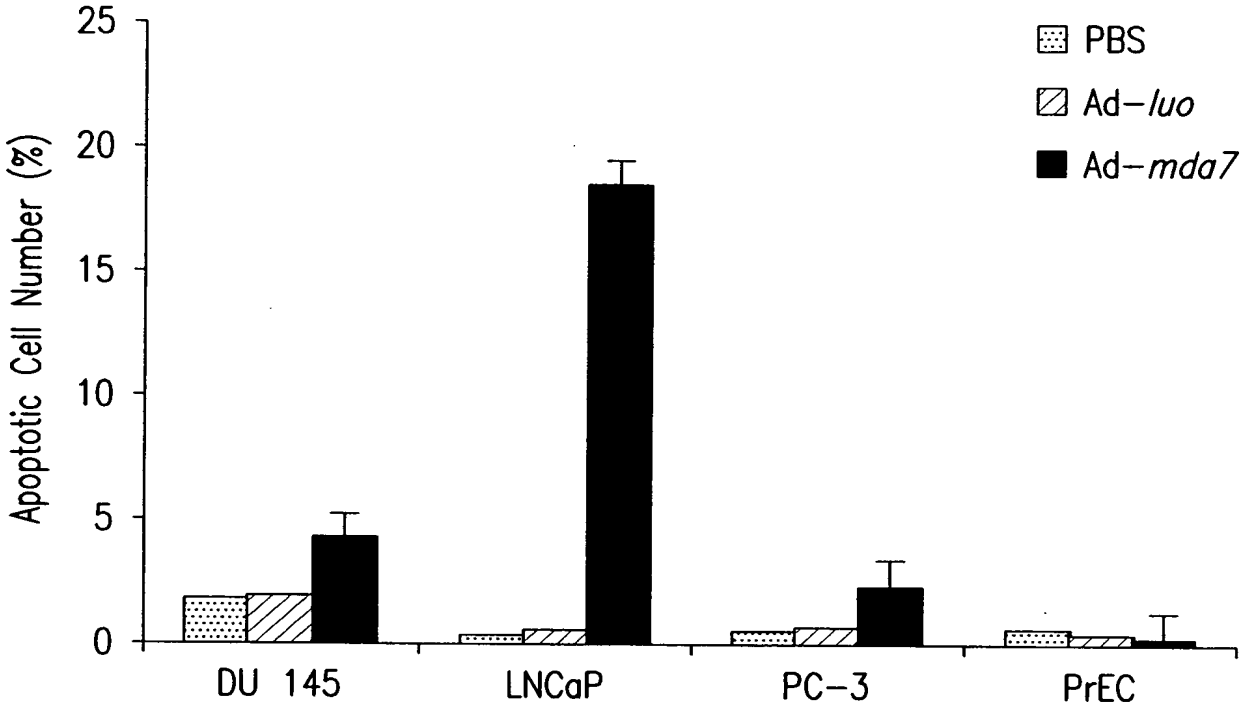

25
20
15
10
5
0
Apoptotic Cell Number (%)
PBS
Ad–luo
Ad–mda7
DU 145
LNCaP
PC–3
PrEC

FIG.17

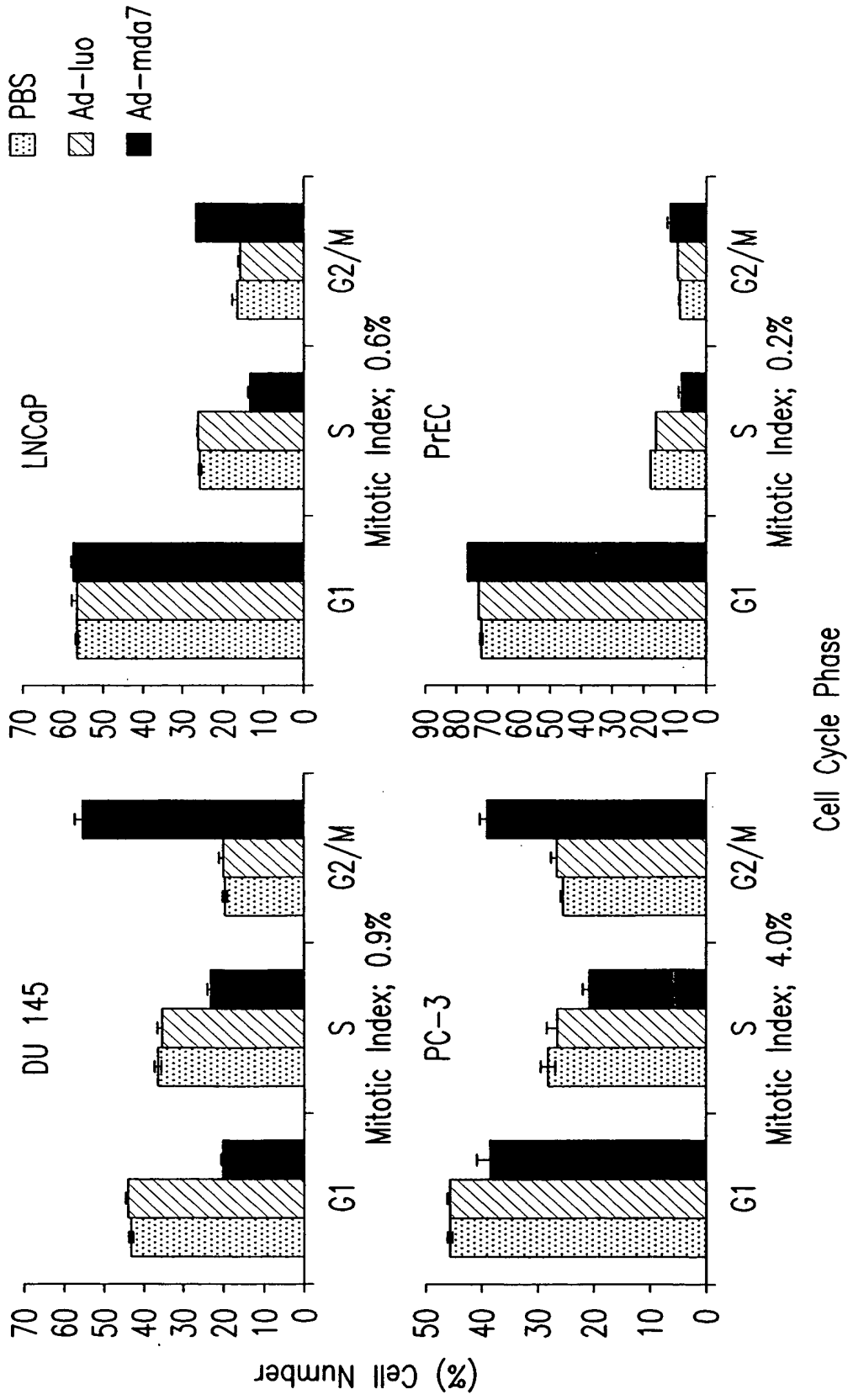

PBS
Ad-luo
Ad-mda7
LNCaP
PrEC
DU 145
PC-3
Mitotic Index; 0.6%
Mitotic Index; 0.2%
Mitotic Index; 0.9%
Mitotic Index; 4.0%
G1
S
G2/M
(%) Cell Number
Cell Cycle Phase

FIG.18

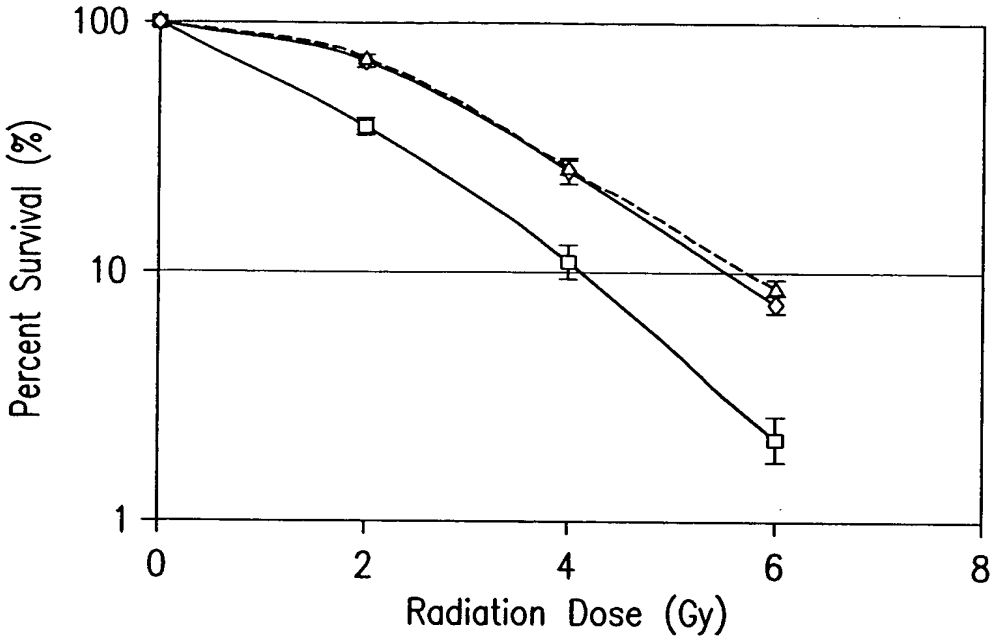


FIG.19A

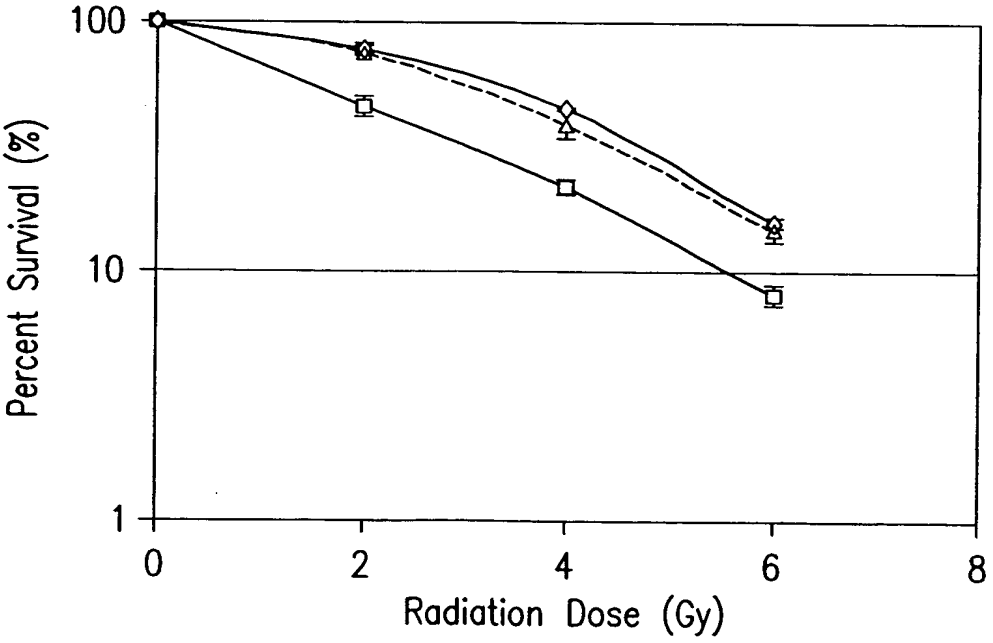


FIG.19B

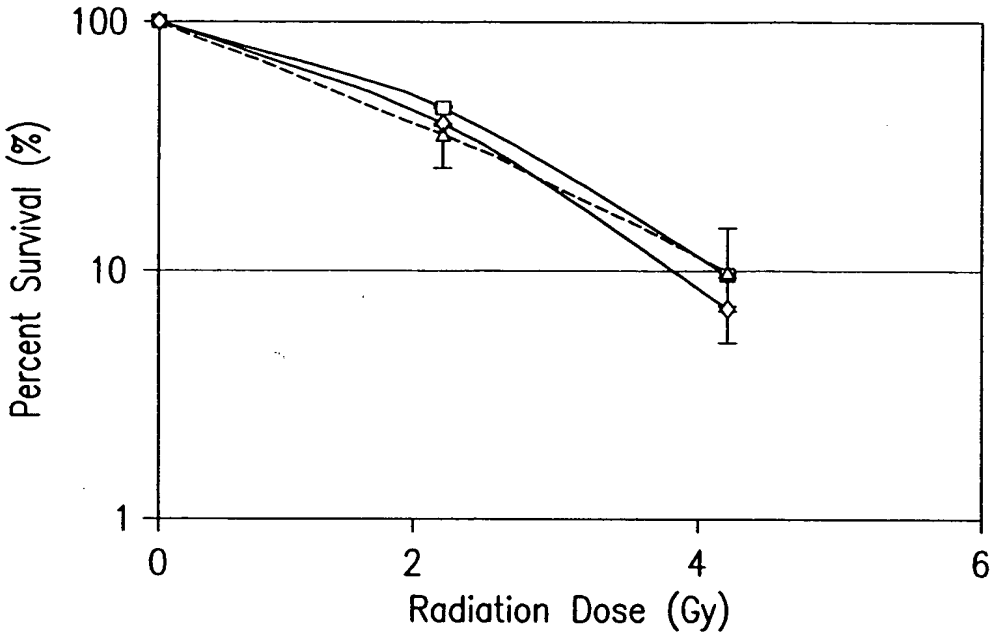


FIG.19C

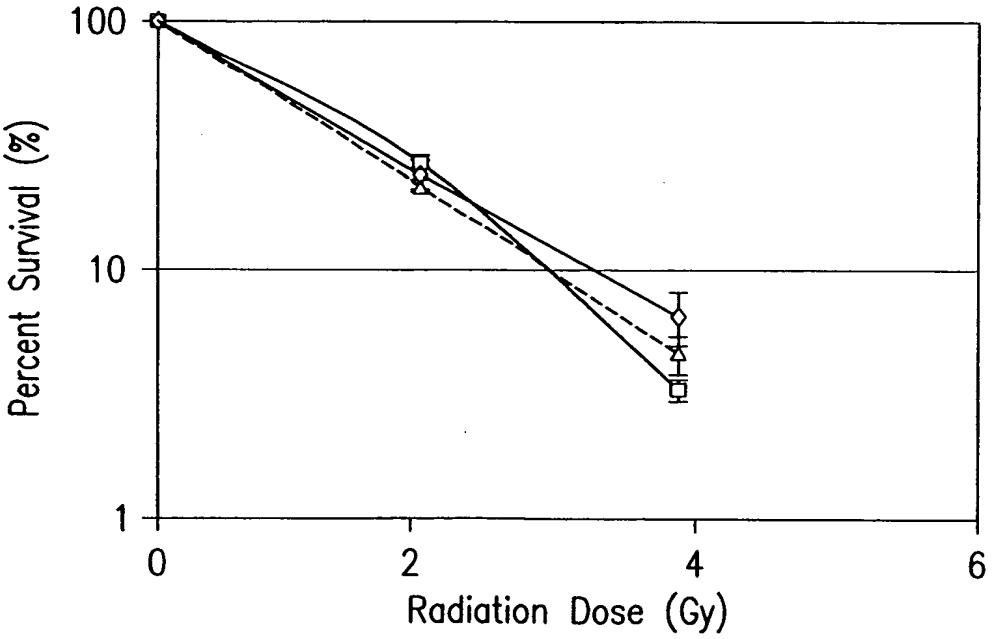


FIG.19D

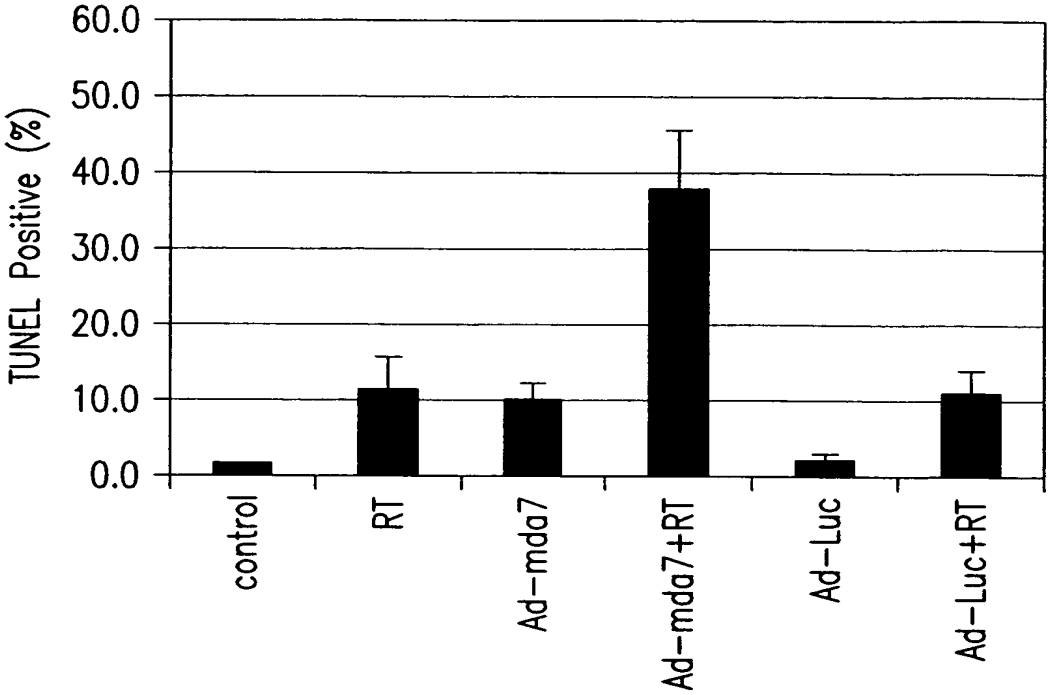


FIG.20A

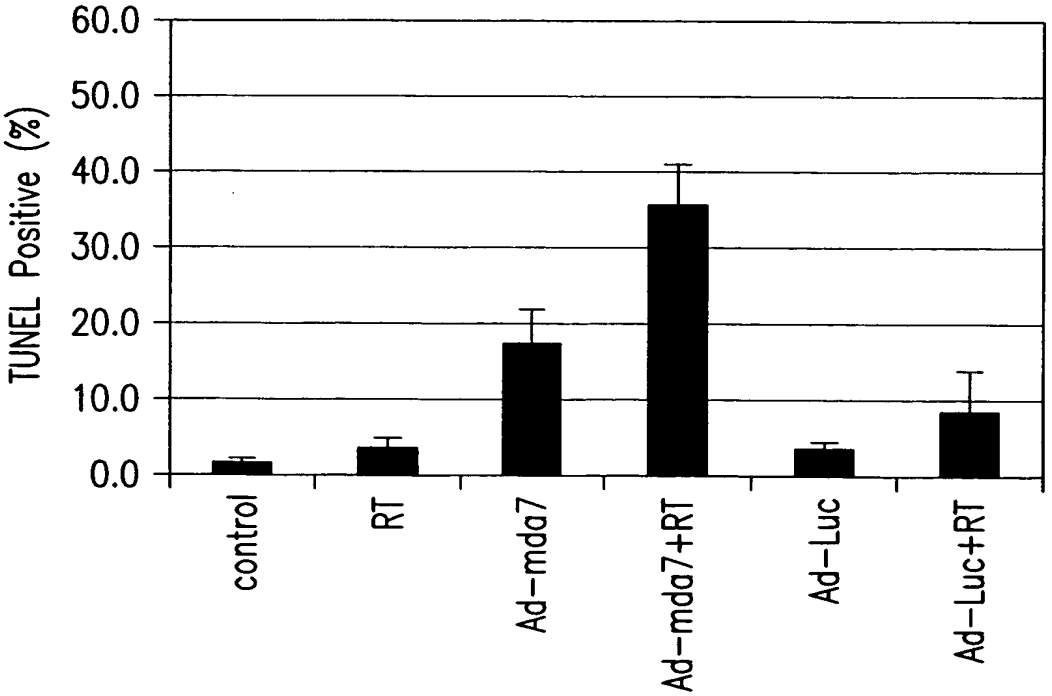


FIG.20B

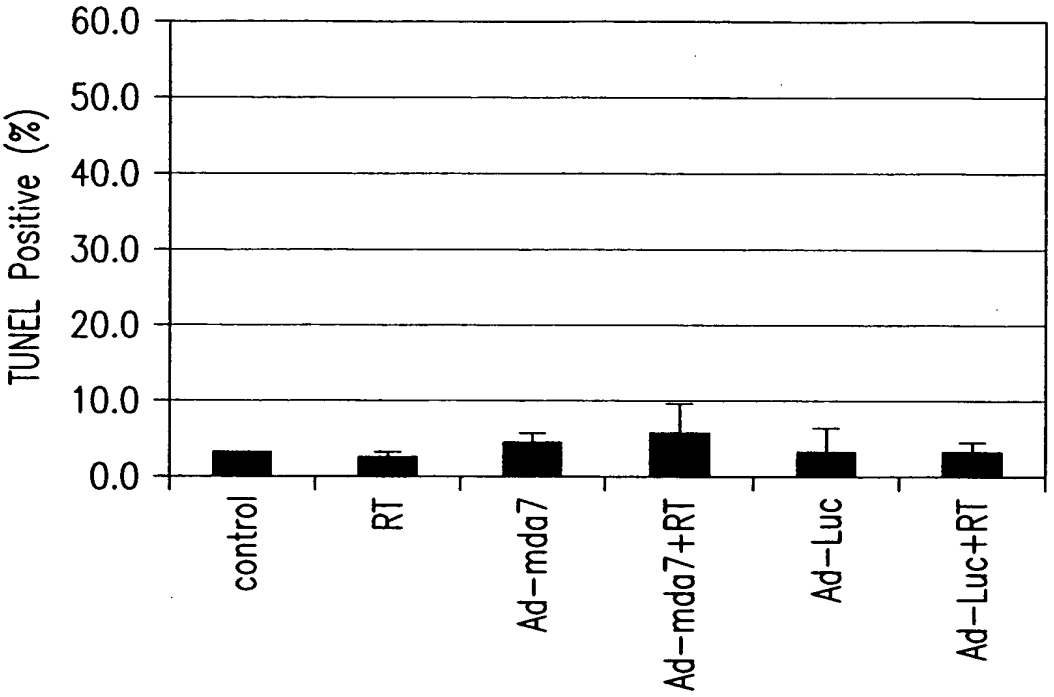


FIG.20C

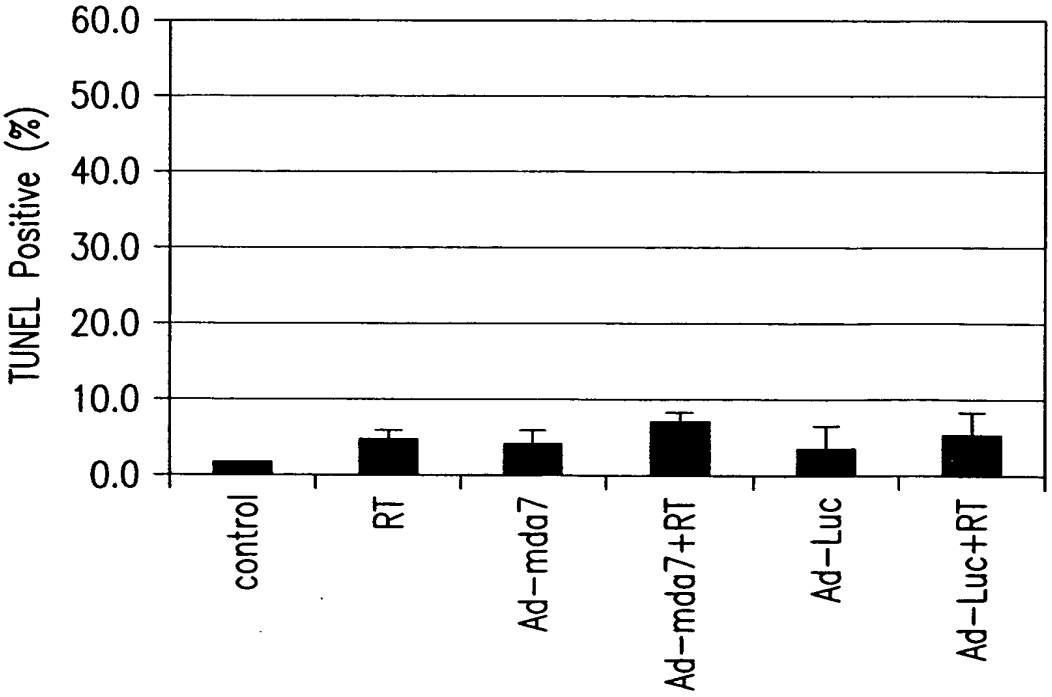


FIG.20D

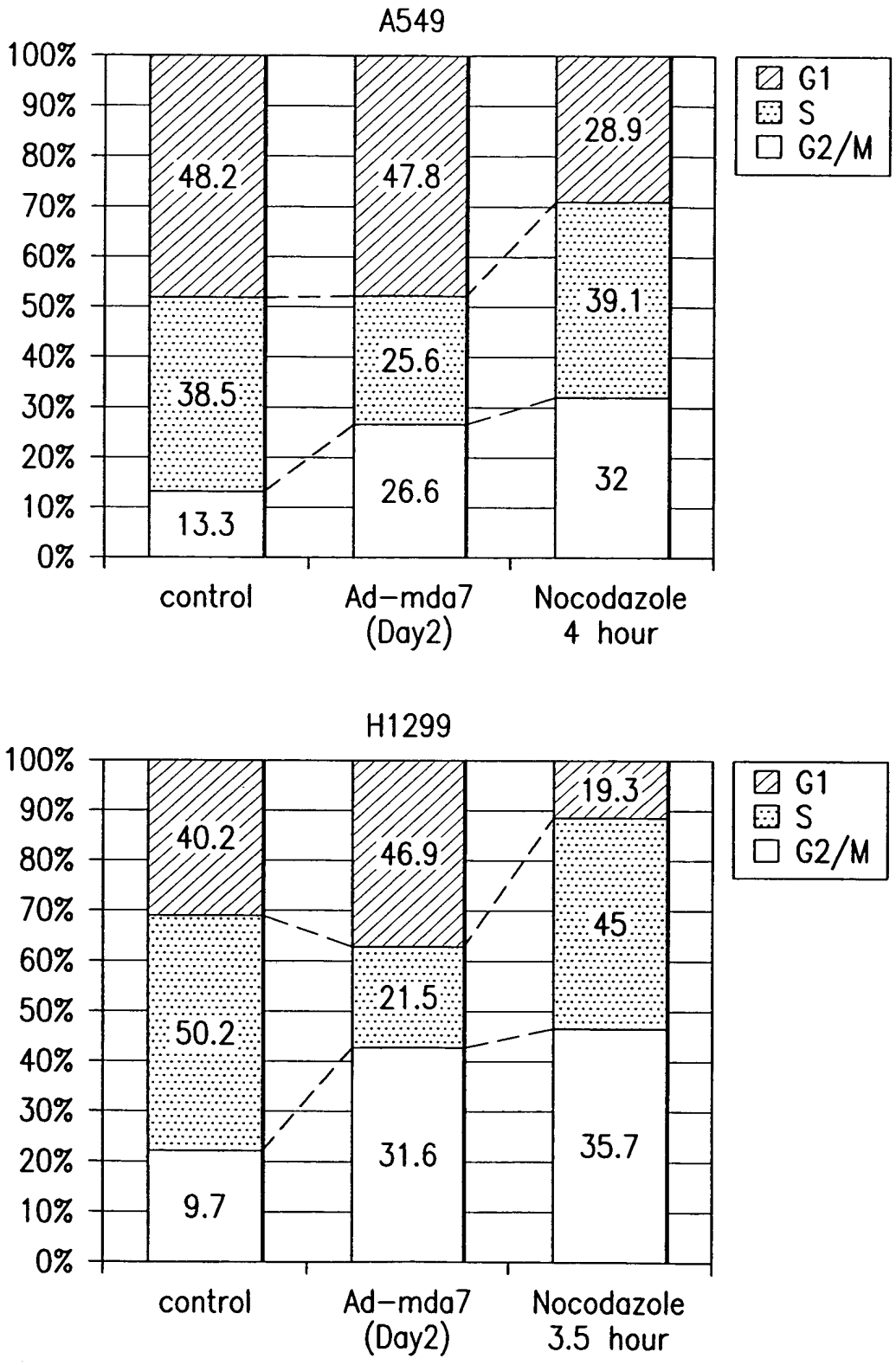
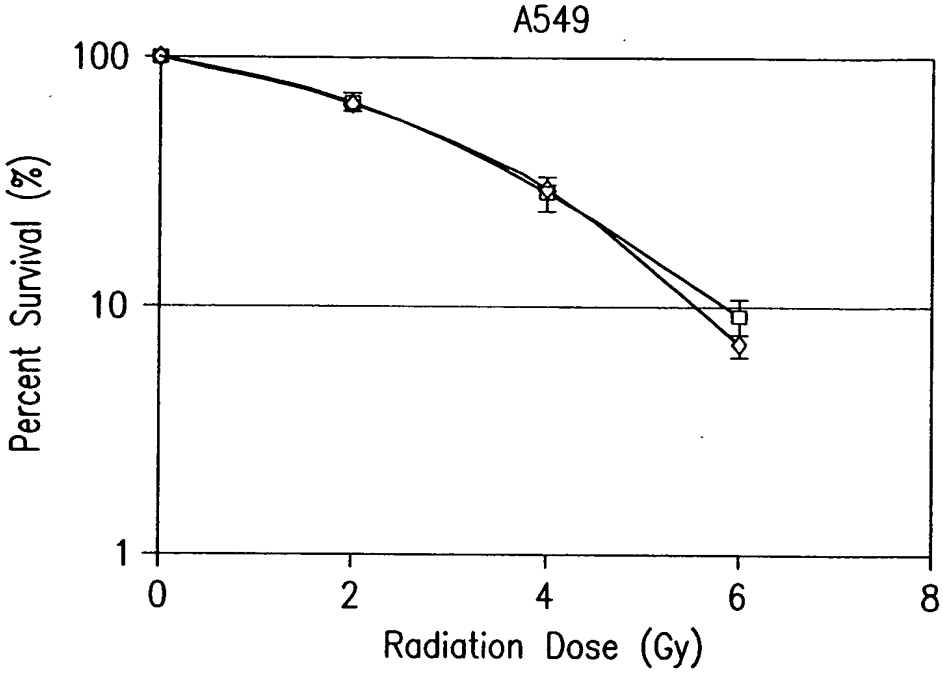

A549
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
48.2
38.5
13.3
47.8
25.6
26.6
28.9
39.1
32
G1
S
G2/M
control
Ad-mda7
(Day2)
Nocodazole
4 hour
H1299
40.2
50.2
9.7
46.9
21.5
31.6
19.3
45
35.7
control
Ad-mda7
(Day2)
Nocodazole
3.5 hour

FIG.21


A549
100
10
1
Percent Survival (%)
0
2
4
6
8
Radiation Dose (Gy)

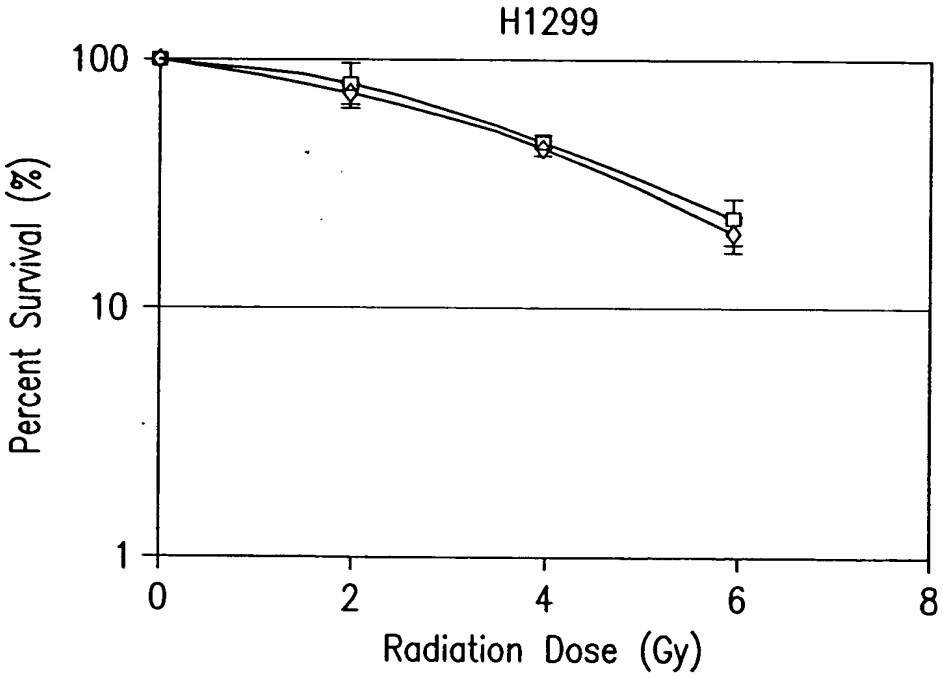
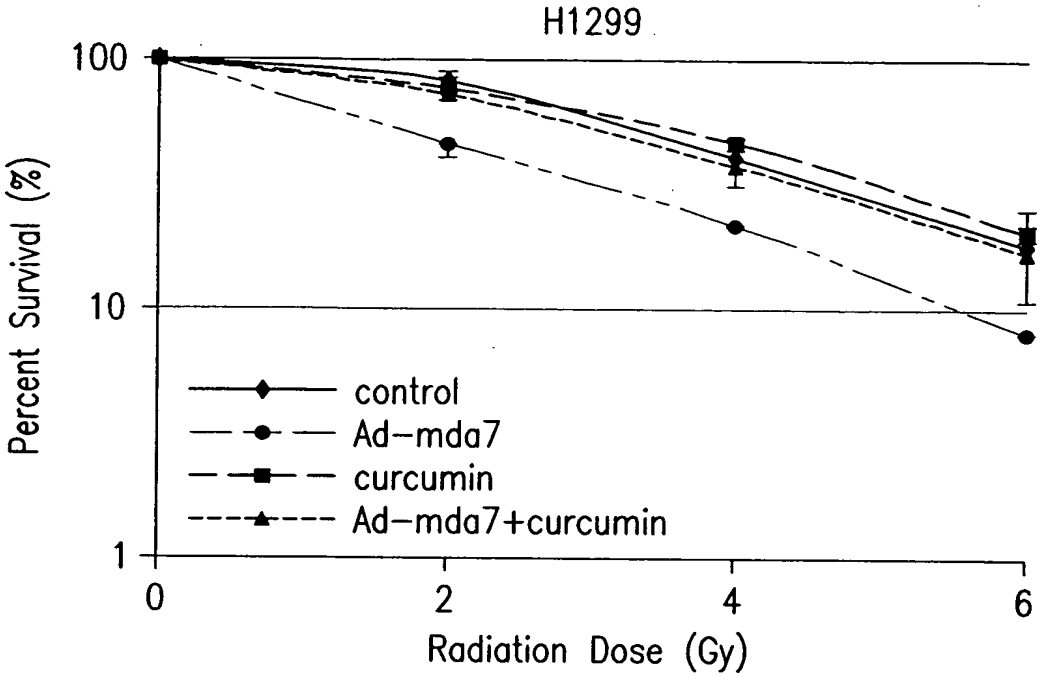

H1299
100
10
1
Percent Survival (%)
0
2
4
6
8
Radiation Dose (Gy)

FIG.22


H1299
100
10
1
Percent Survival (%)
0
2
4
6
Radiation Dose (Gy)
control
Ad-mda7
curcumin
Ad-mda7+curcumin

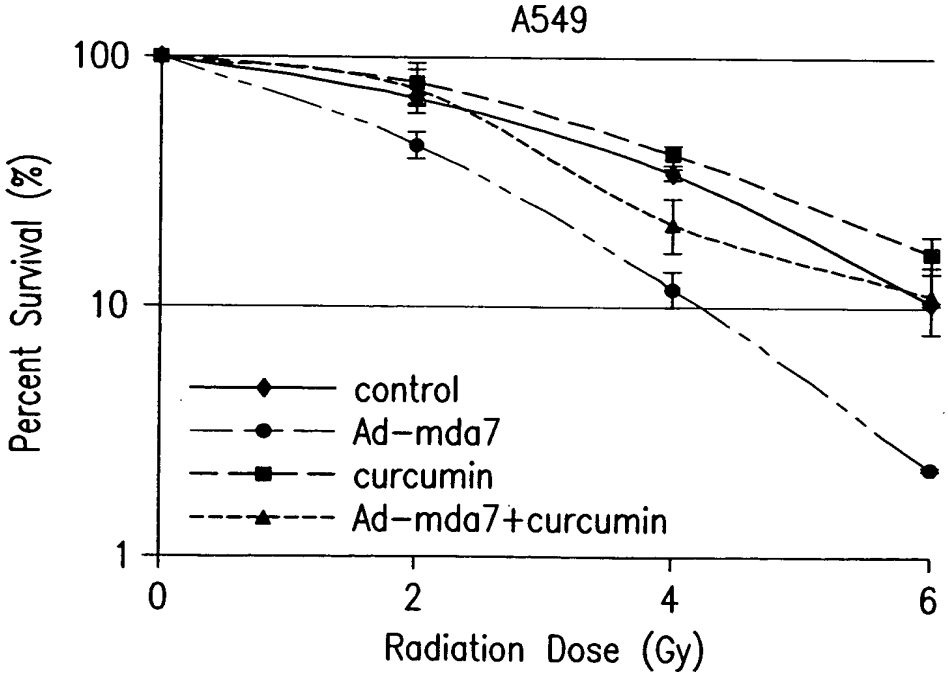

A549
100
10
1
Percent Survival (%)
0
2
4
6
Radiation Dose (Gy)
control
Ad-mda7
curcumin
Ad-mda7+curcumin

FIG.23

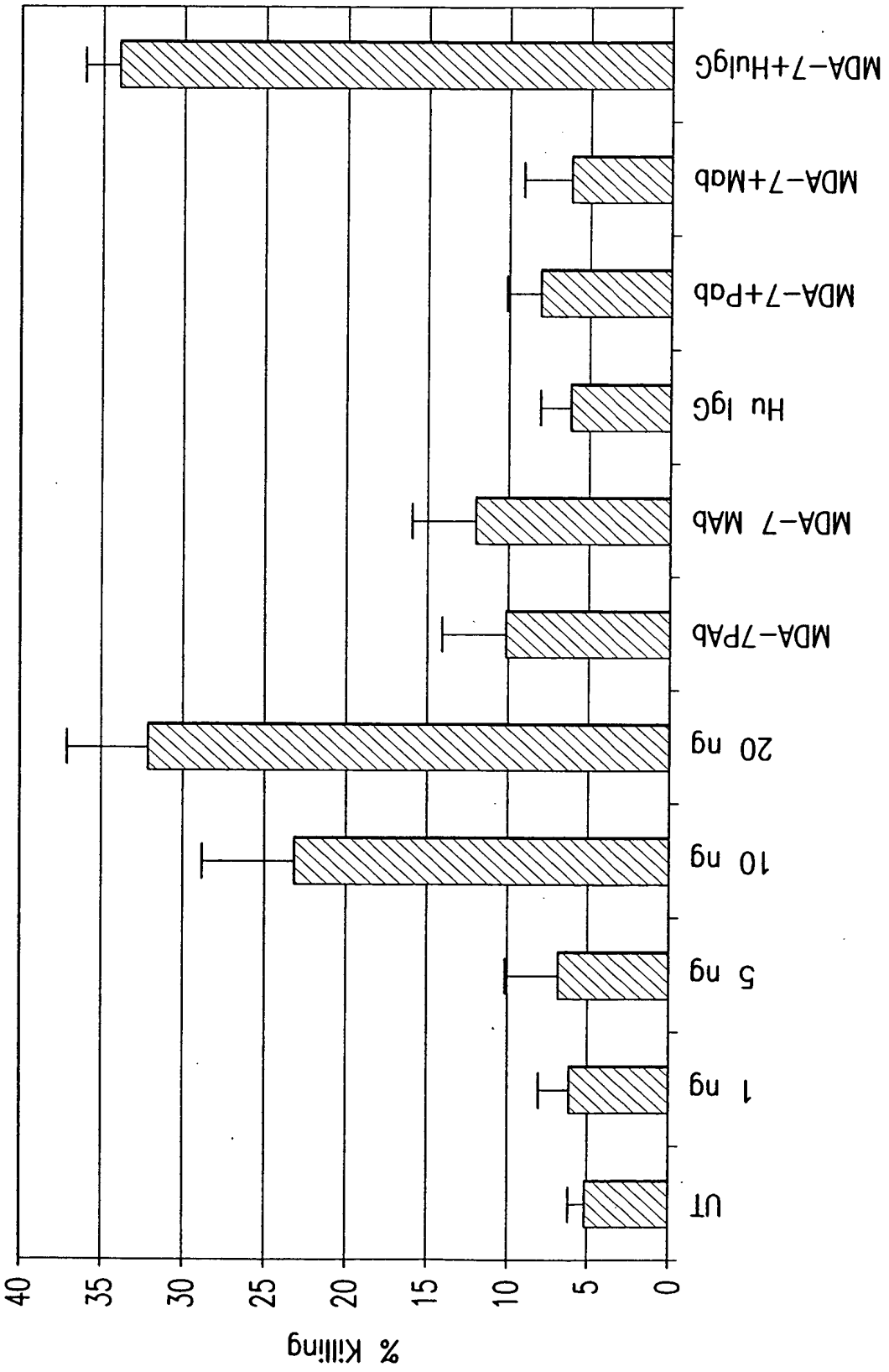
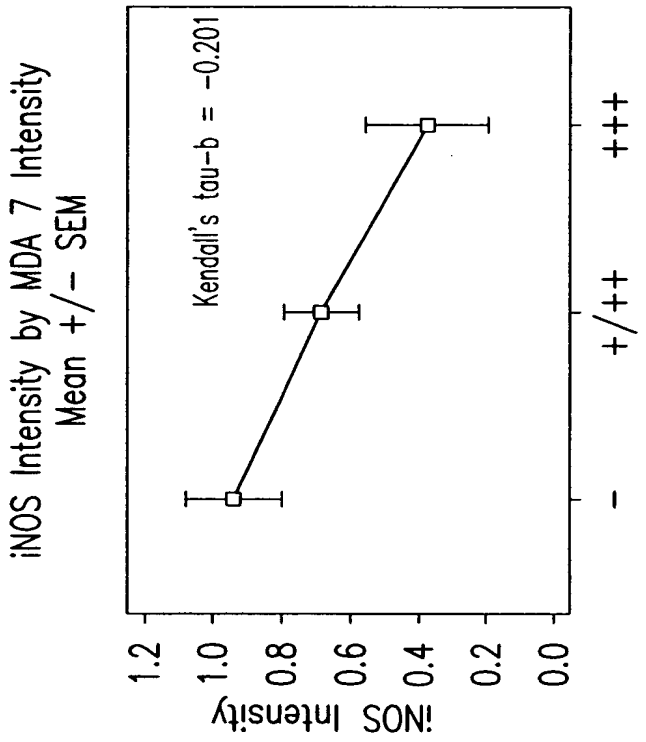
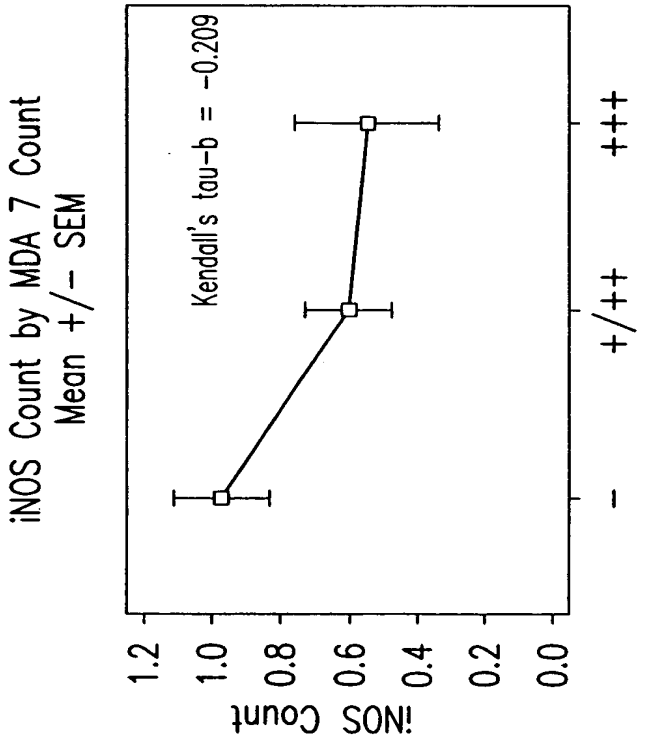

% Killing
0
5
10
15
20
25
30
35
40
UT
1 ng
5 ng
10 ng
20 ng
MDA-7PAb
MDA-7 MAb
Hu IgG
MDA-7+Pab
MDA-7+Mab
MDA-7+HuIgG

FIG.24



MDA-7 count	Average iNOS count	SE	N
-	1.21	.16	32
+/++	.90	.14	41
+++	.50	.27	8

FIG.25B



MDA-7 count	Average iNOS count	SE	N
-	.97	.13	35
+/++	.60	.12	35
+++	.54	.21	11

FIG.25A

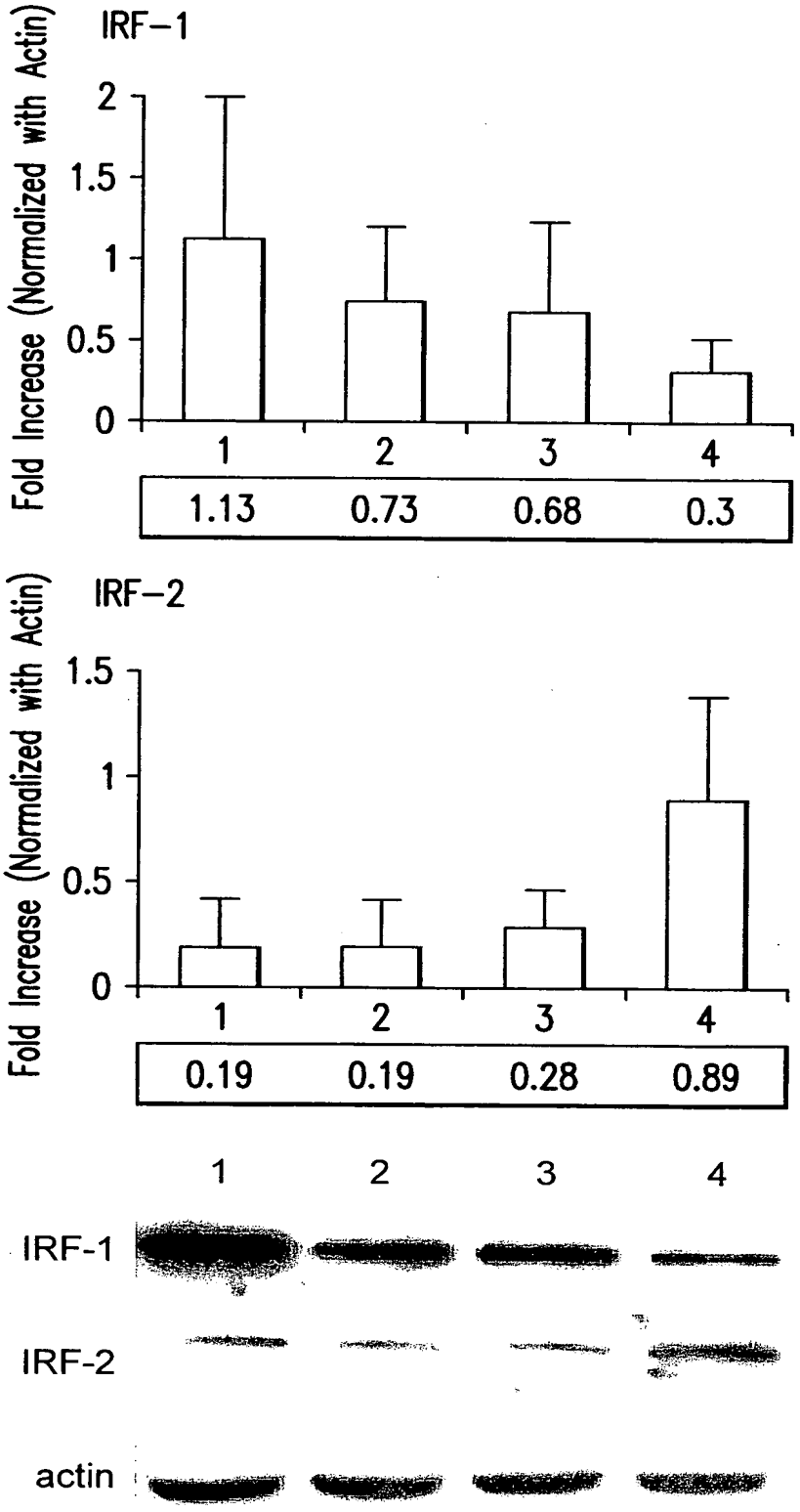

IRF-1
Fold Increase (Normalized with Actin)
2
1.5
1
0.5
0
1
2
3
4
1.13
0.73
0.68
0.3
IRF-2
Fold Increase (Normalized with Actin)
1.5
1
0.5
0
1
2
3
4
0.19
0.19
0.28
0.89
1
2
3
4
IRF-1
IRF-2
actin

FIG.26

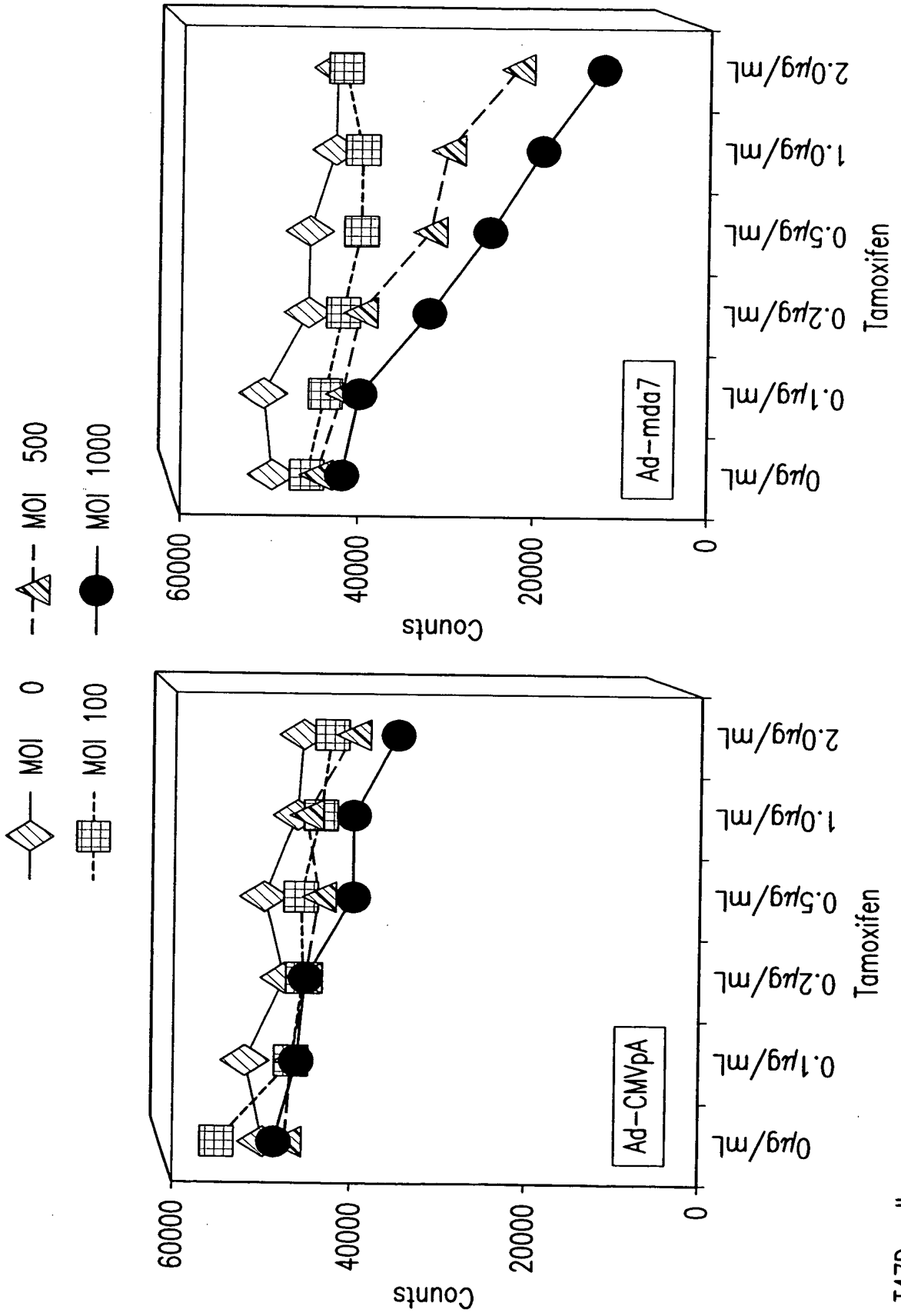

MOI 0
MOI 100
MOI 500
MOI 1000
Counts
60000
40000
20000
0
Ad-CMVpA
Ad-mda7
0μg/mL
0.1μg/mL
0.2μg/mL
0.5μg/mL
1.0μg/mL
2.0μg/mL
Tamoxifen
T47D cells

FIG.27

	IL-6	IFN-g	IL-10	GM-CSF	s.Fas	IL-1b	TNF-a	pSTAT3
Ad-mda7	++	++	decrease	+/-	++	-	-	++
MDA-7	+	+++	decrease	n.d.	n.d.	n.d.	n.d.	++

+->+++: increased cytokine secretion compared to Ad-luc control
-: no change; n.d.: not done.
Cytokine levels were evaluated using ELISA from cultured cell supernatants taken 24-72 hr post treatment.
pSTAT3 results were analyzed 4hr after addition of MDA-7 protein and 24 hr after Ad-mda7 treatment using IHC.

FIG.28

Replacement Sheet

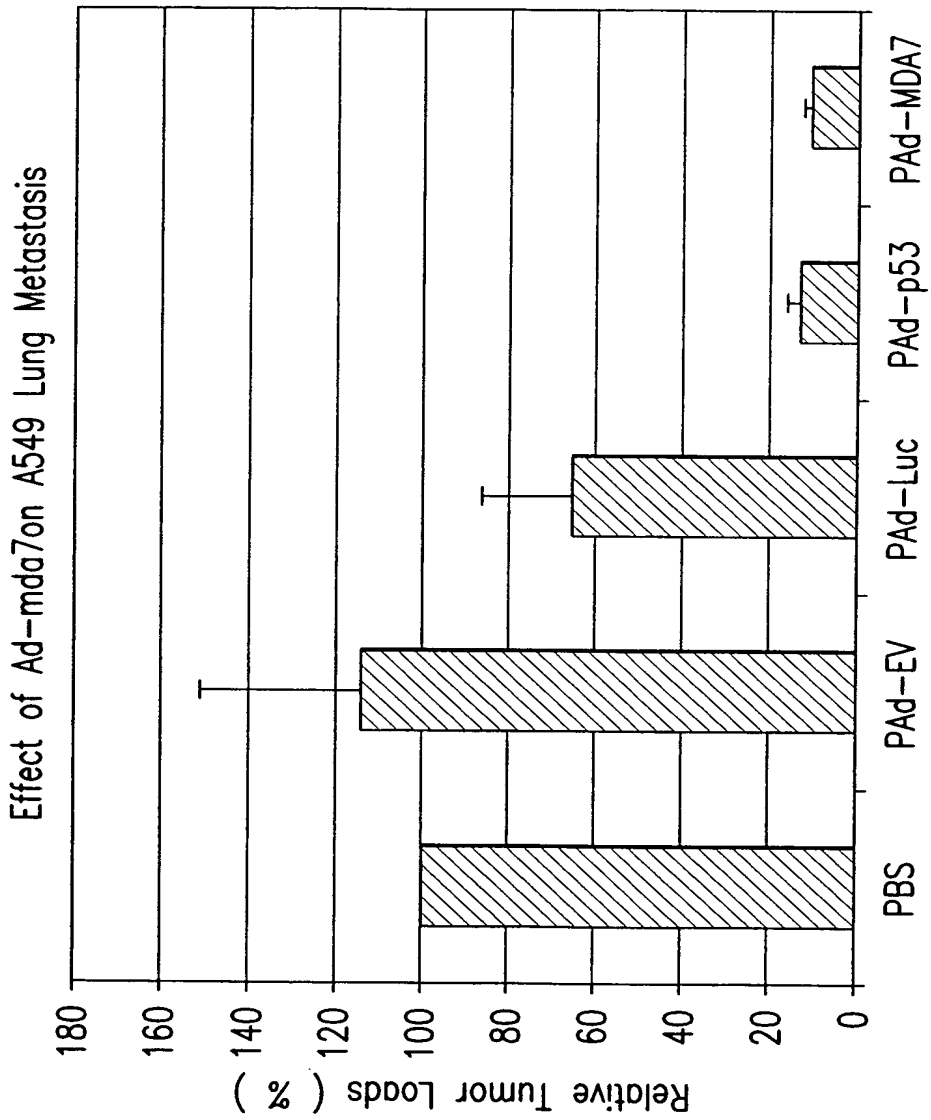

Effect of Ad-mda7on A549 Lung Metastasis
Relative Tumor Loads (%)
0
20
40
60
80
100
120
140
160
180
PBS
PAd-EV
PAd-Luc
PAd-p53
PAd-MDA7

FIG.29

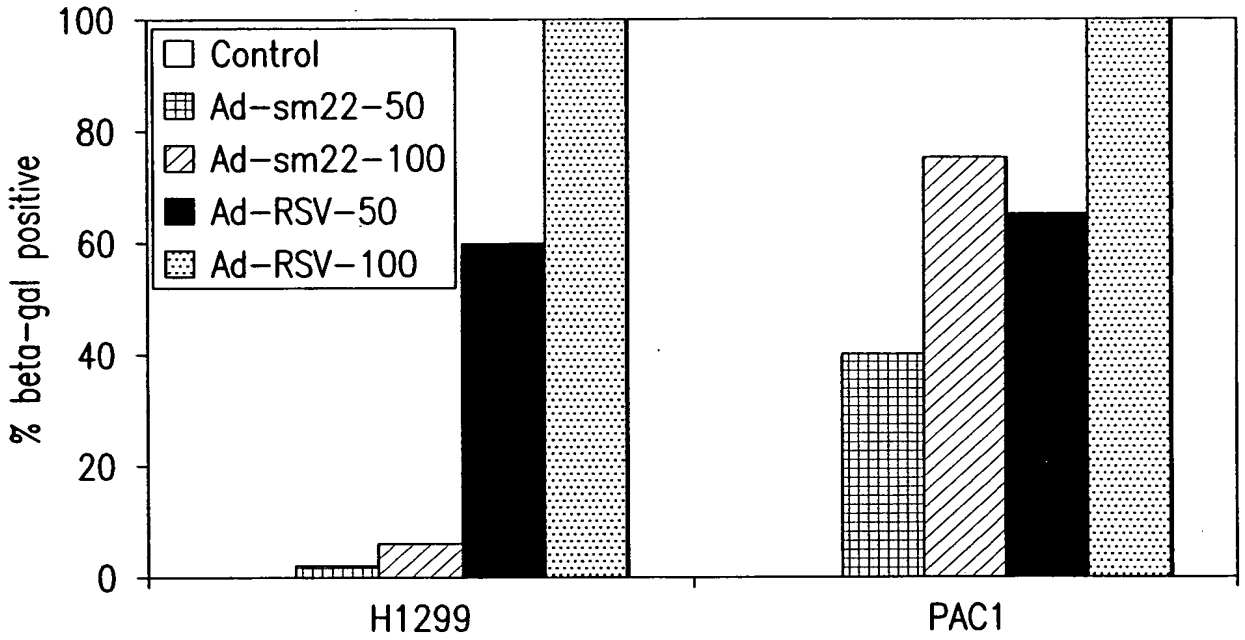

100
80
60
40
20
0
% beta-gal positive
Control
Ad-sm22-50
Ad-sm22-100
Ad-RSV-50
Ad-RSV-100
H1299
PAC1

FIG.30

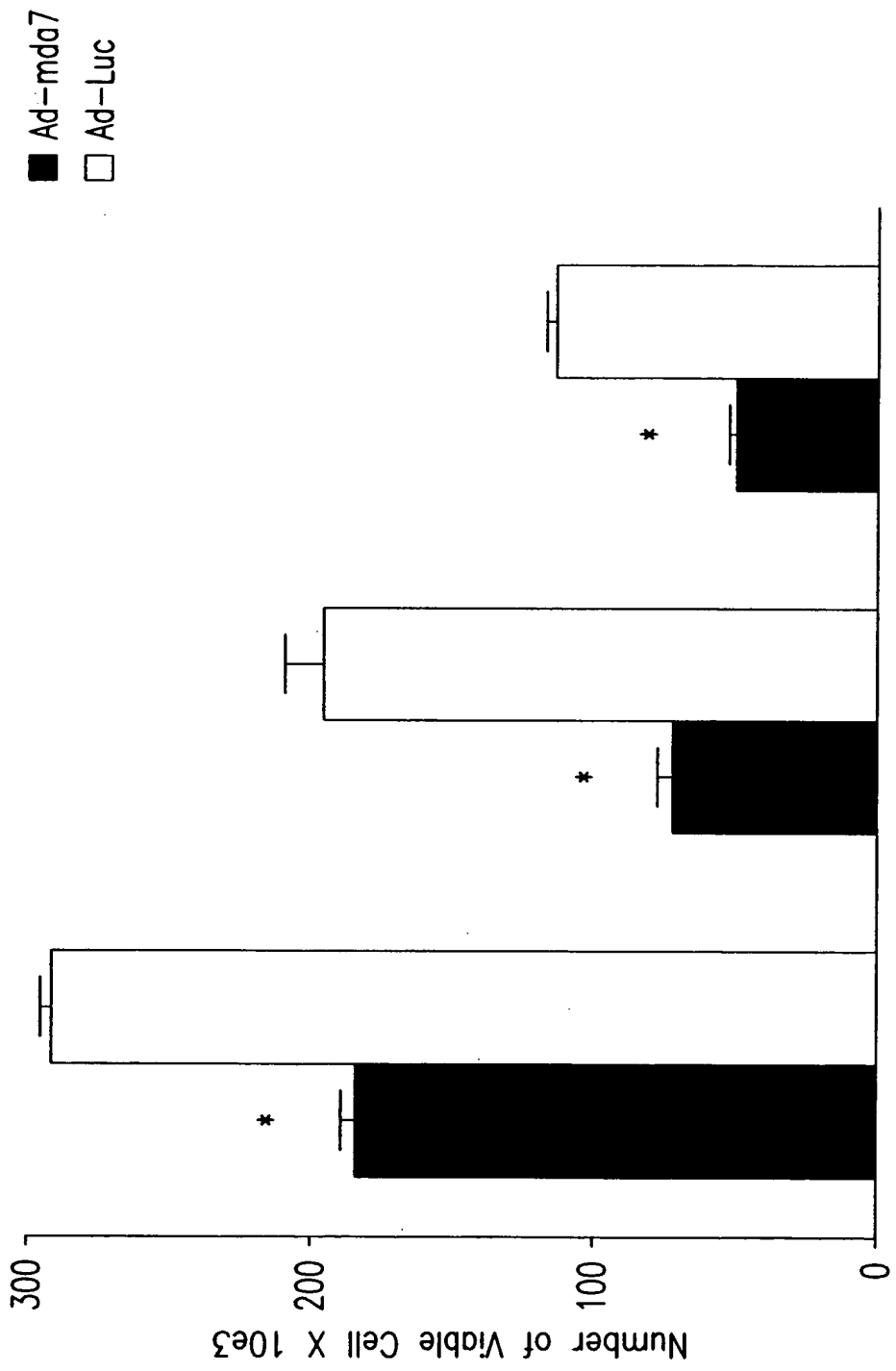

Ad-mda7
Ad-Luc
Number of Viable Cell X 10e3
300
200
100
0
*
*
*
40 MOI
100 MOI
200 MOI

FIG.31

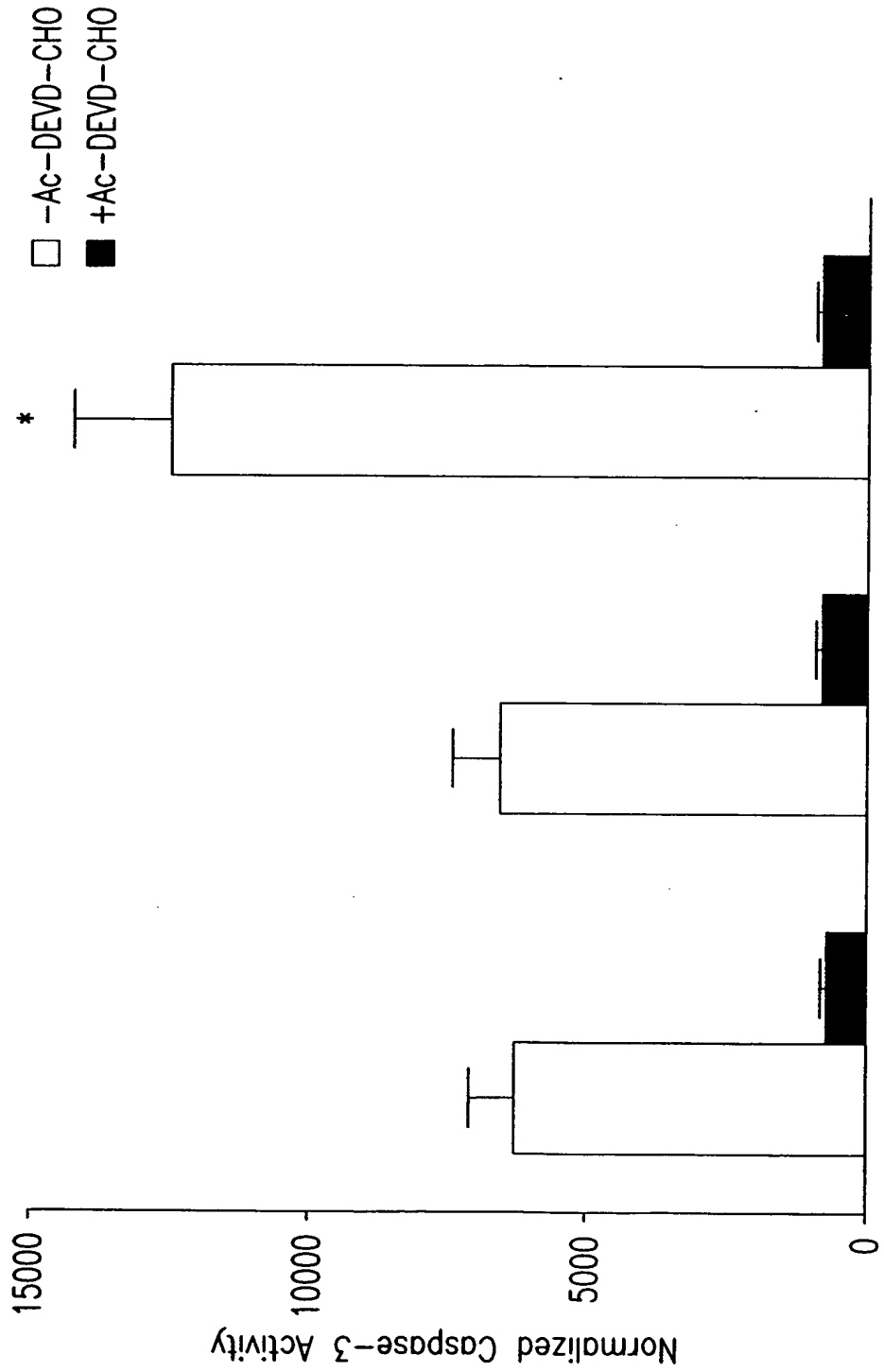

Normalized Caspase-3 Activity
15000
10000
5000
0
Control
Ad-Luc
Ad-mda7
*
-Ac-DEVD-CHO
+Ac-DEVD-CHO

FIG.32A

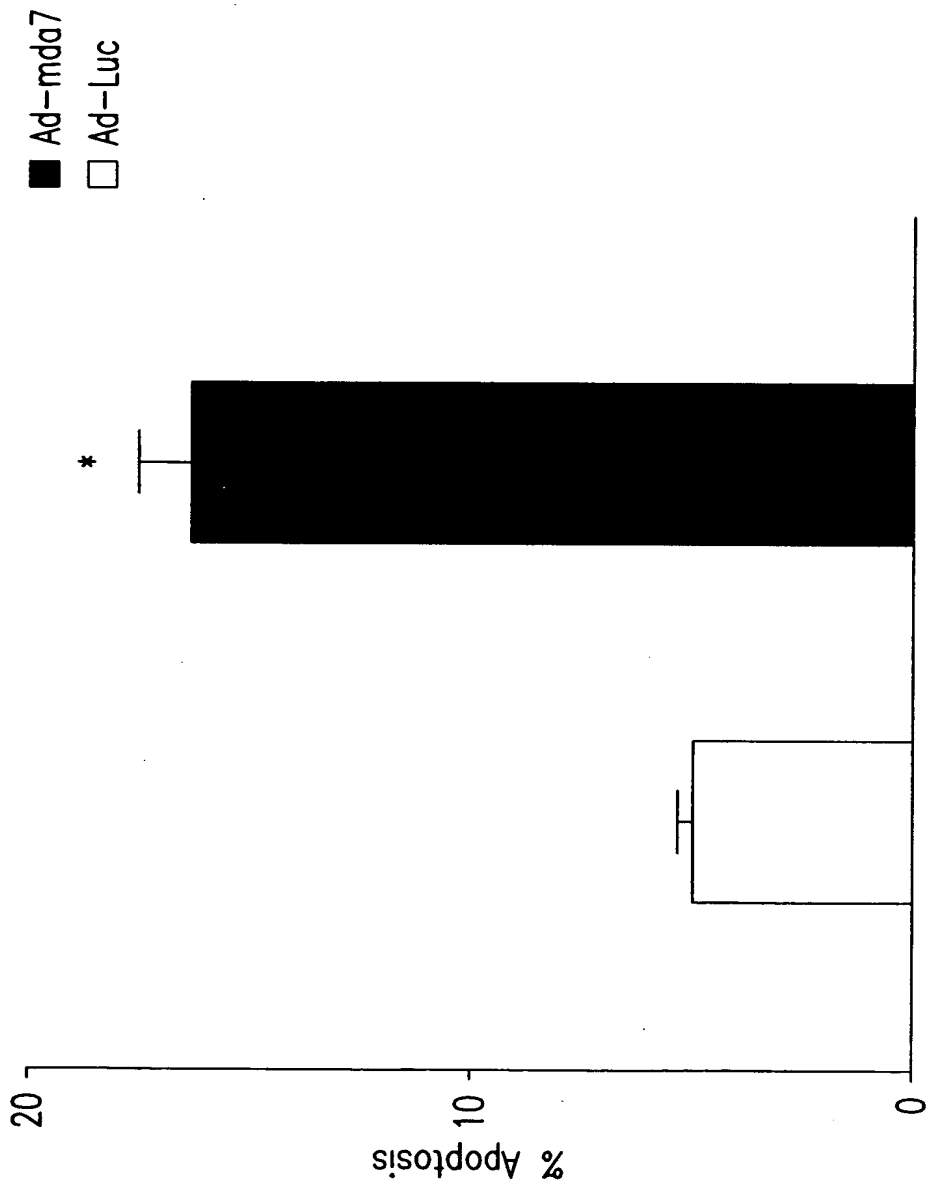


FIG.32B

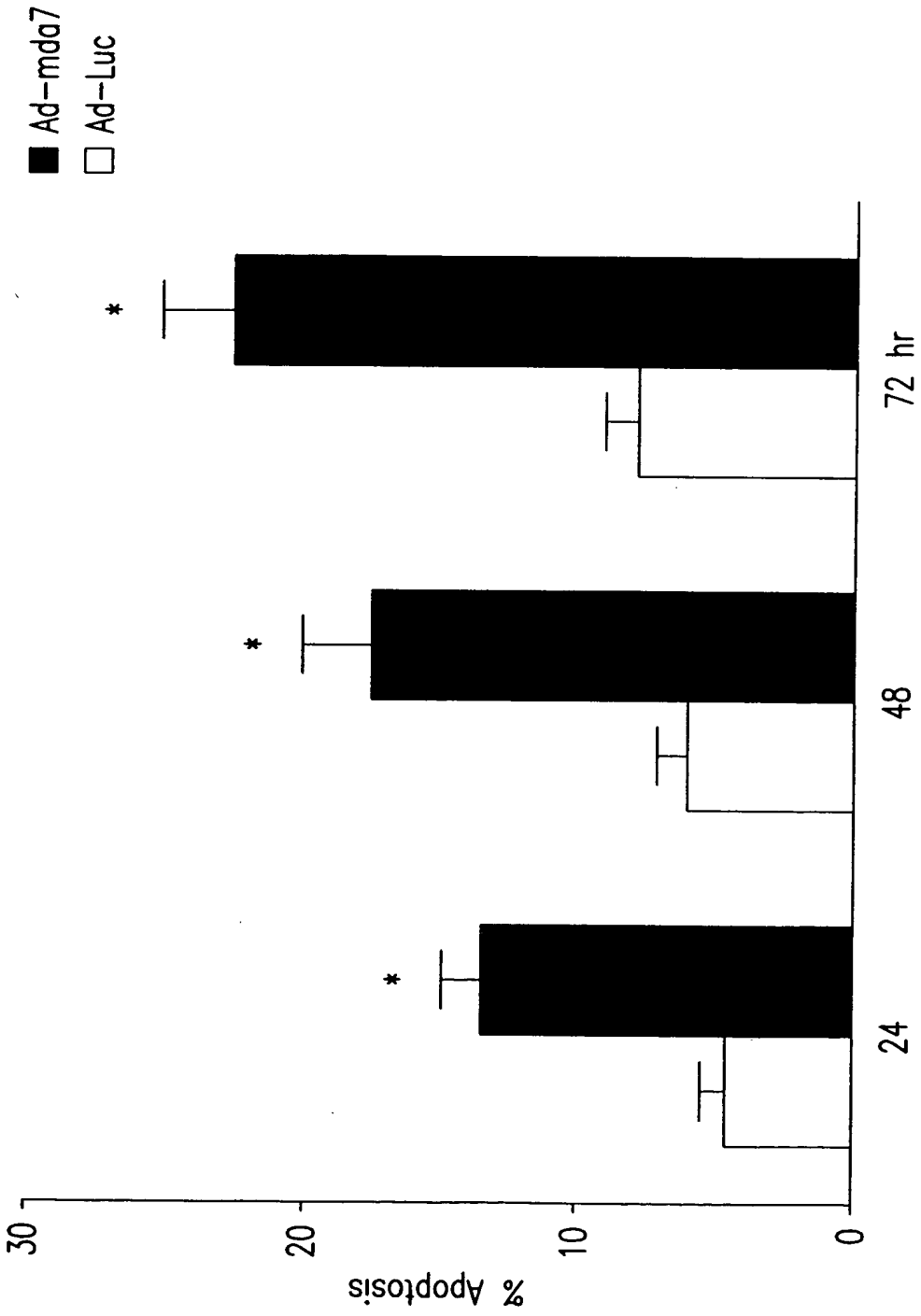


FIG.32C

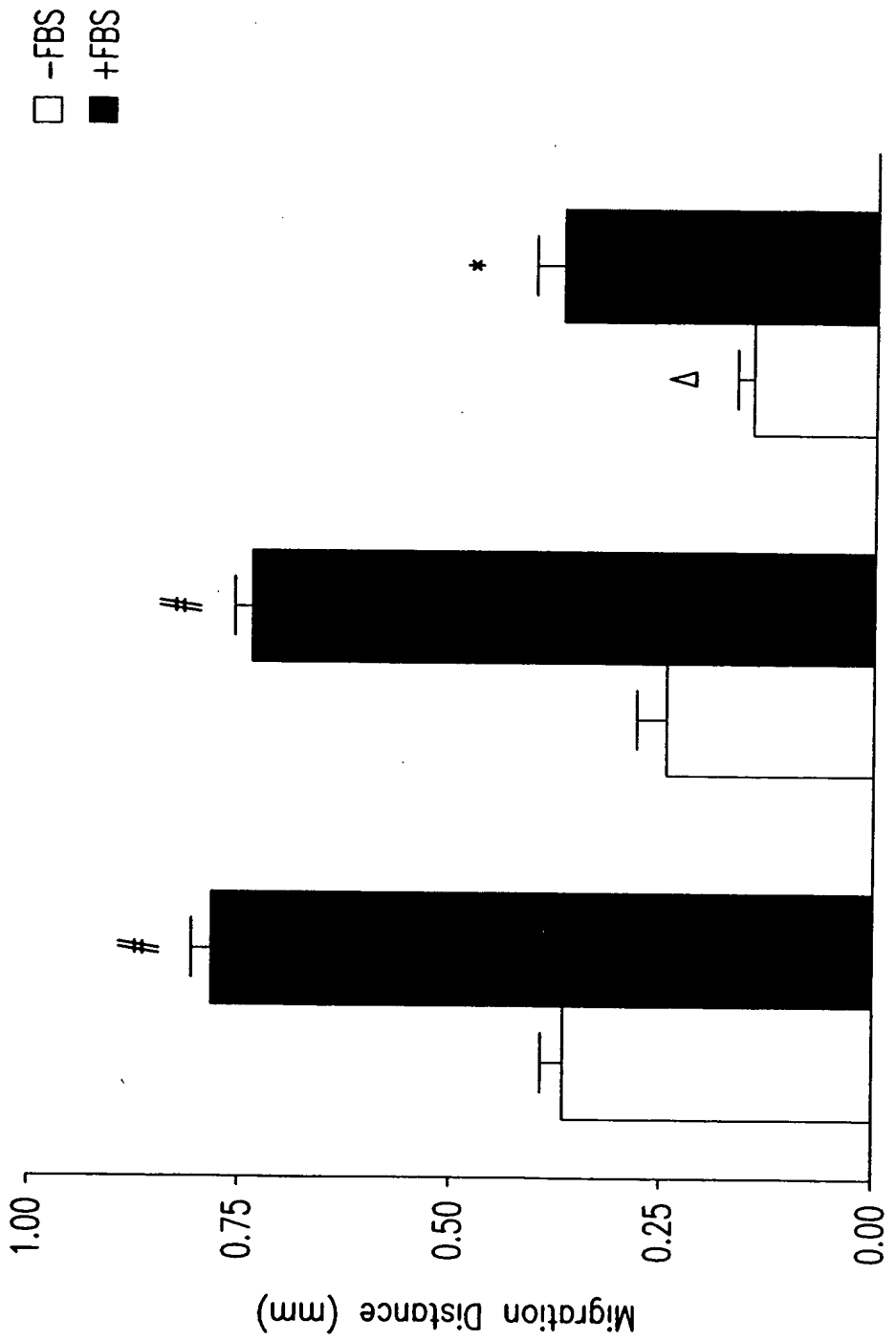

□ -FBS
■ +FBS
Migration Distance (mm)
1.00
0.75
0.50
0.25
0.00
Control
Ad-Luc
Ad-mda7
#
#
Δ
*

FIG.33

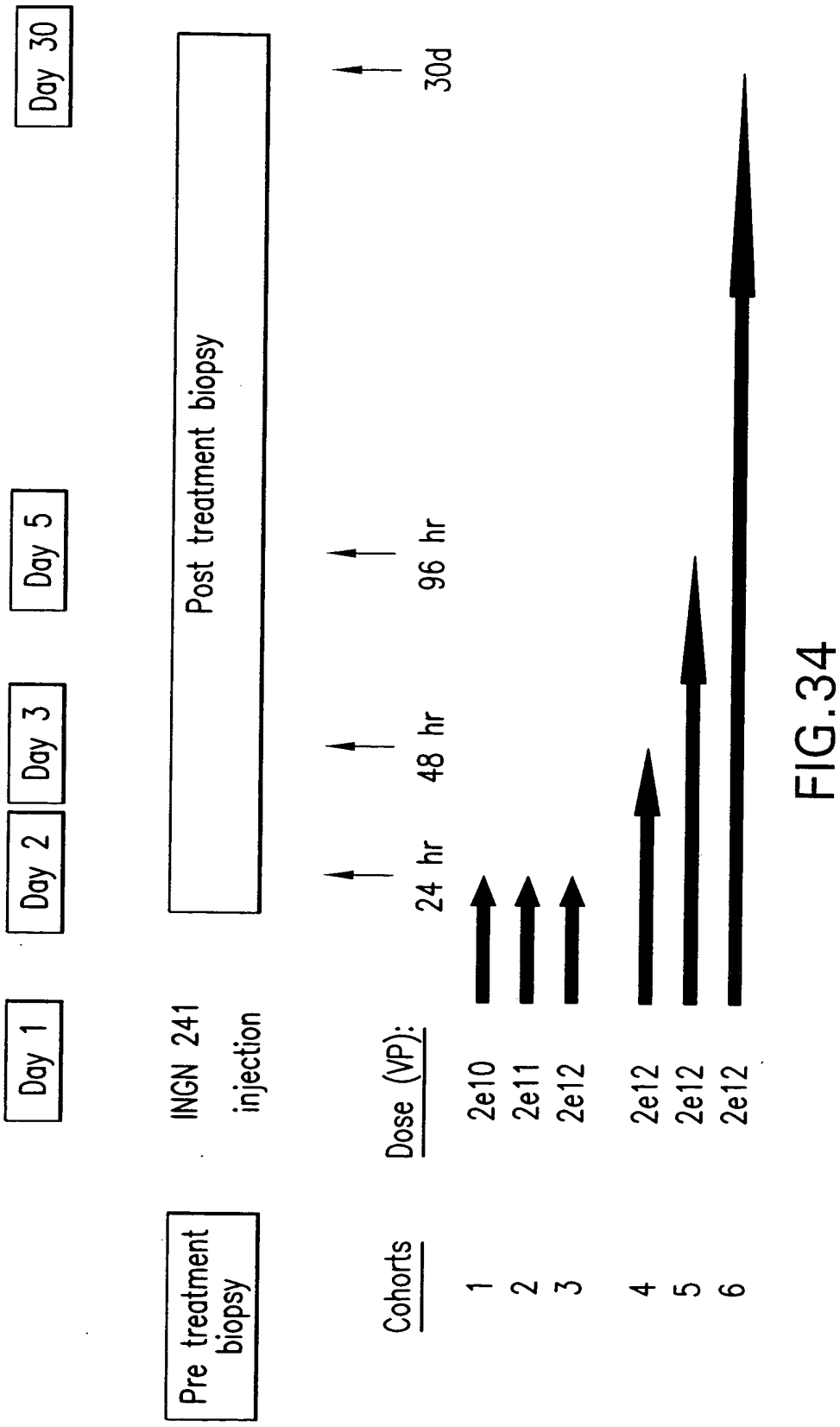

Day 1
Day 2
Day 3
Day 5
Day 30
Pre treatment biopsy
INGN 241 injection
Post treatment biopsy
24 hr
48 hr
96 hr
30d
Cohorts
Dose (VP):
1 2e10
2 2e11
3 2e12
4 2e12
5 2e12
6 2e12

FIG.34

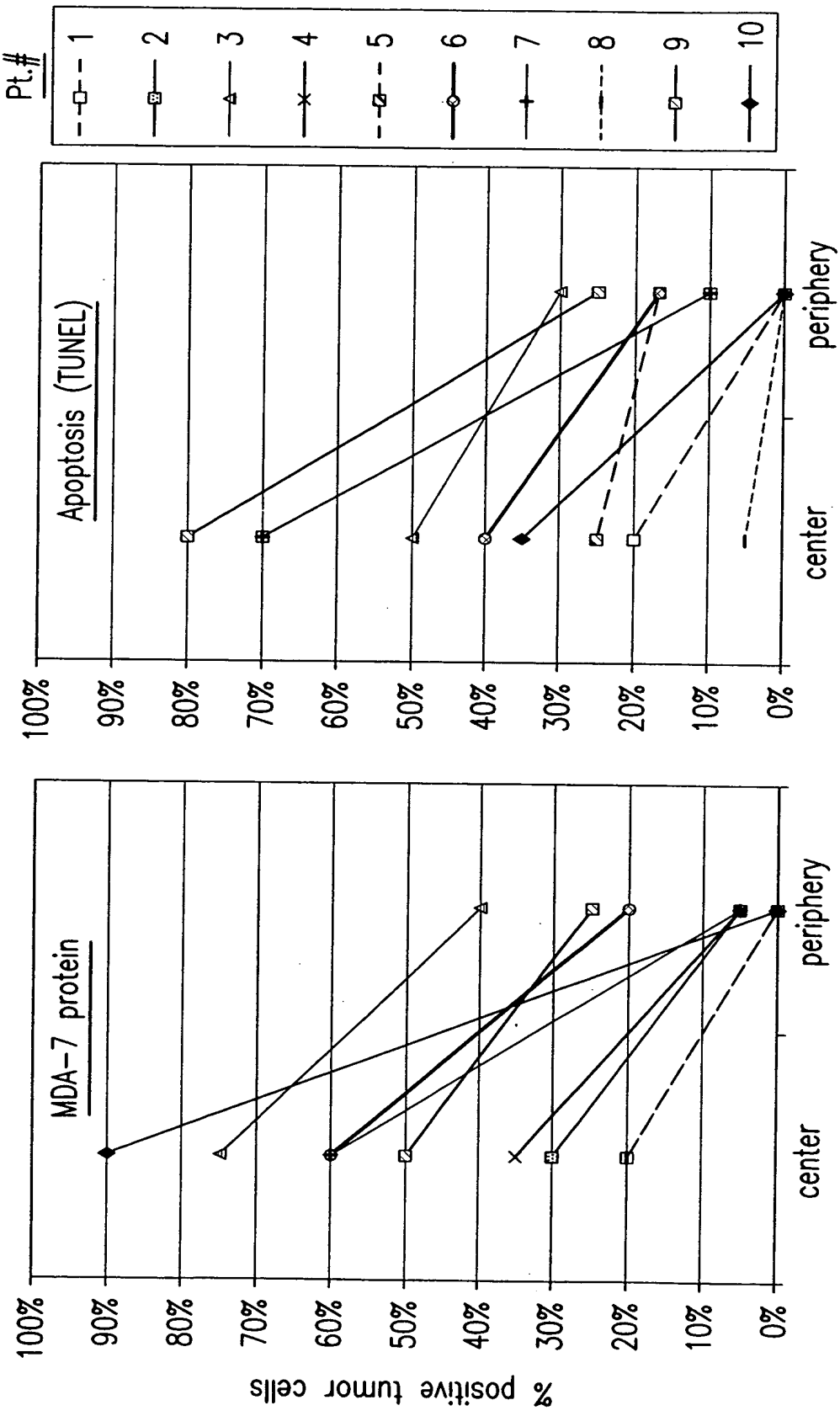
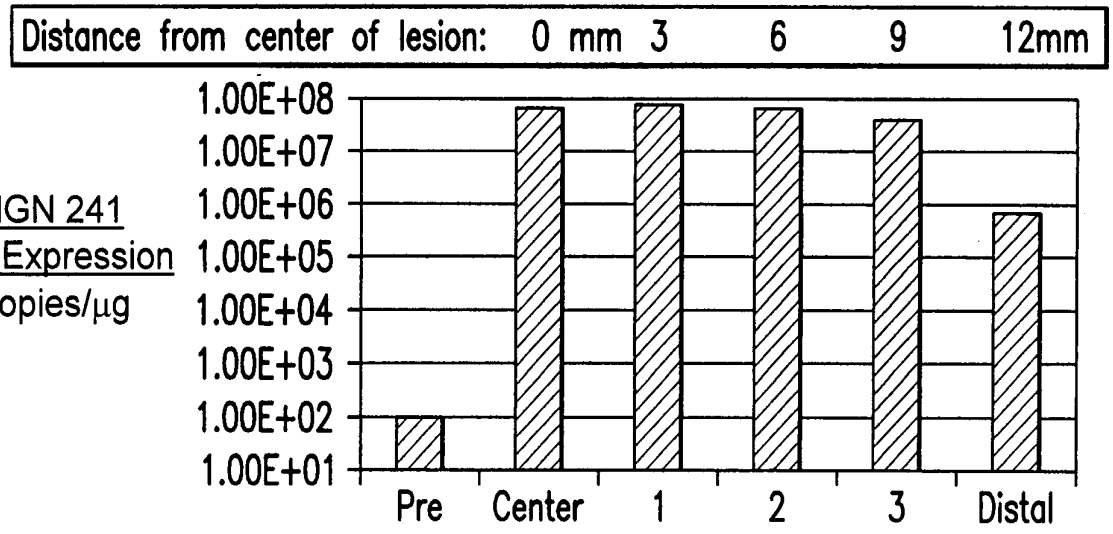
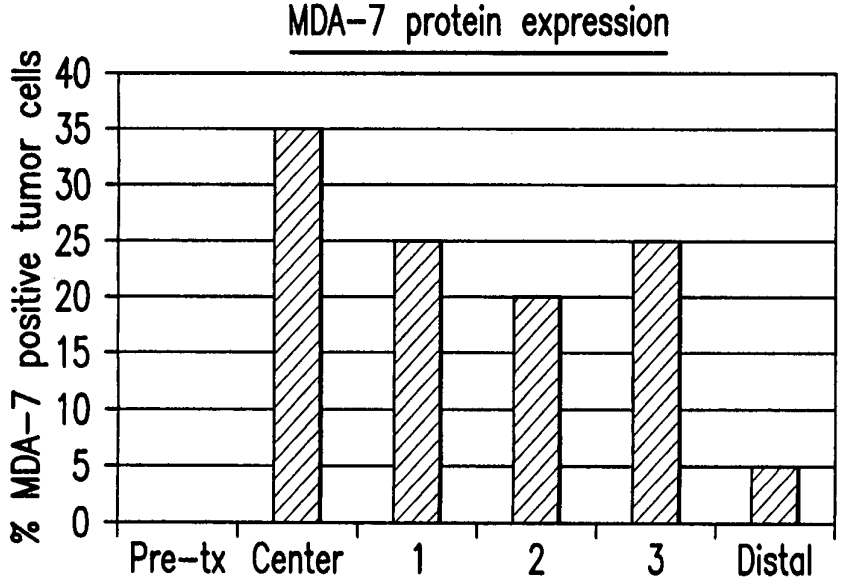

Pt.#
1
2
3
4
5
6
7
8
9
10
Apoptosis (TUNEL)
MDA-7 protein
% positive tumor cells
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
center
periphery
MDA-7/ TUNEL correlation p < 0.01

FIG.35





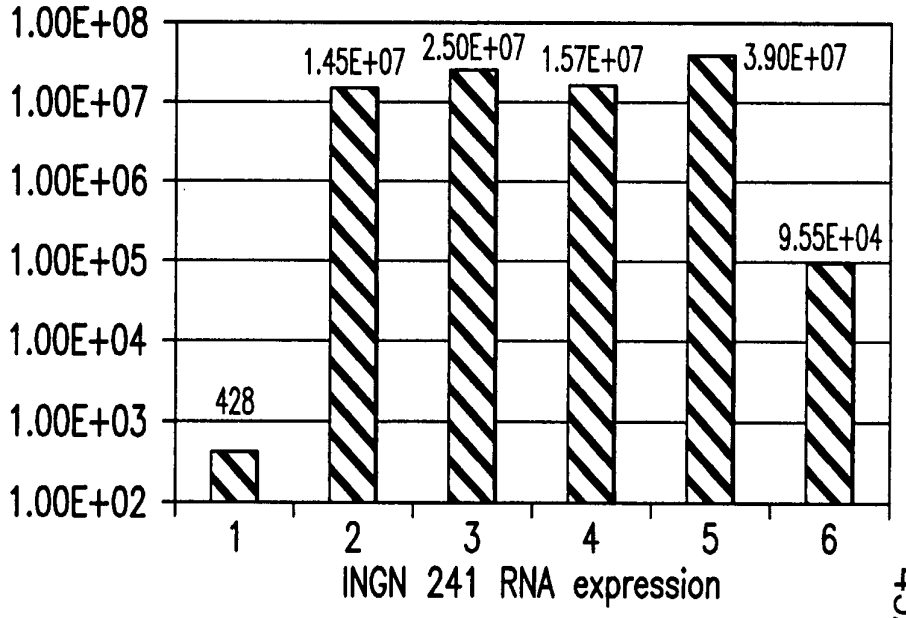


FIG.36

Replacement Sheet

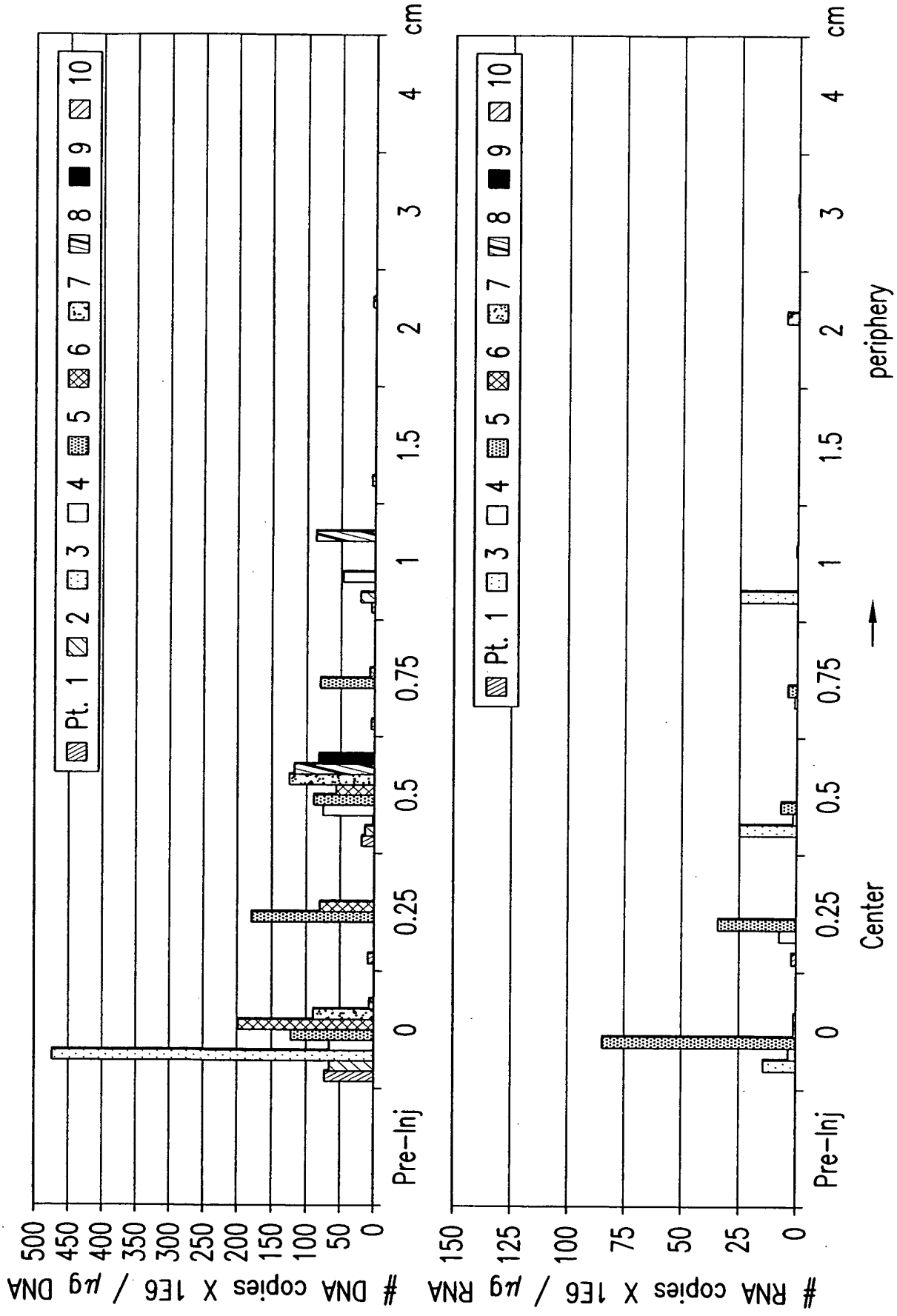

DNA copies X 1E6 / µg DNA
500
450
400
350
300
250
200
150
100
50
0
Pt. 1
2
3
4
5
6
7
8
9
10
Pre-Inj
0
0.25
0.5
0.75
1
1.5
2
3
4
cm
RNA copies X 1E6 / µg RNA
150
125
100
75
50
25
0
Center
periphery

FIG.37

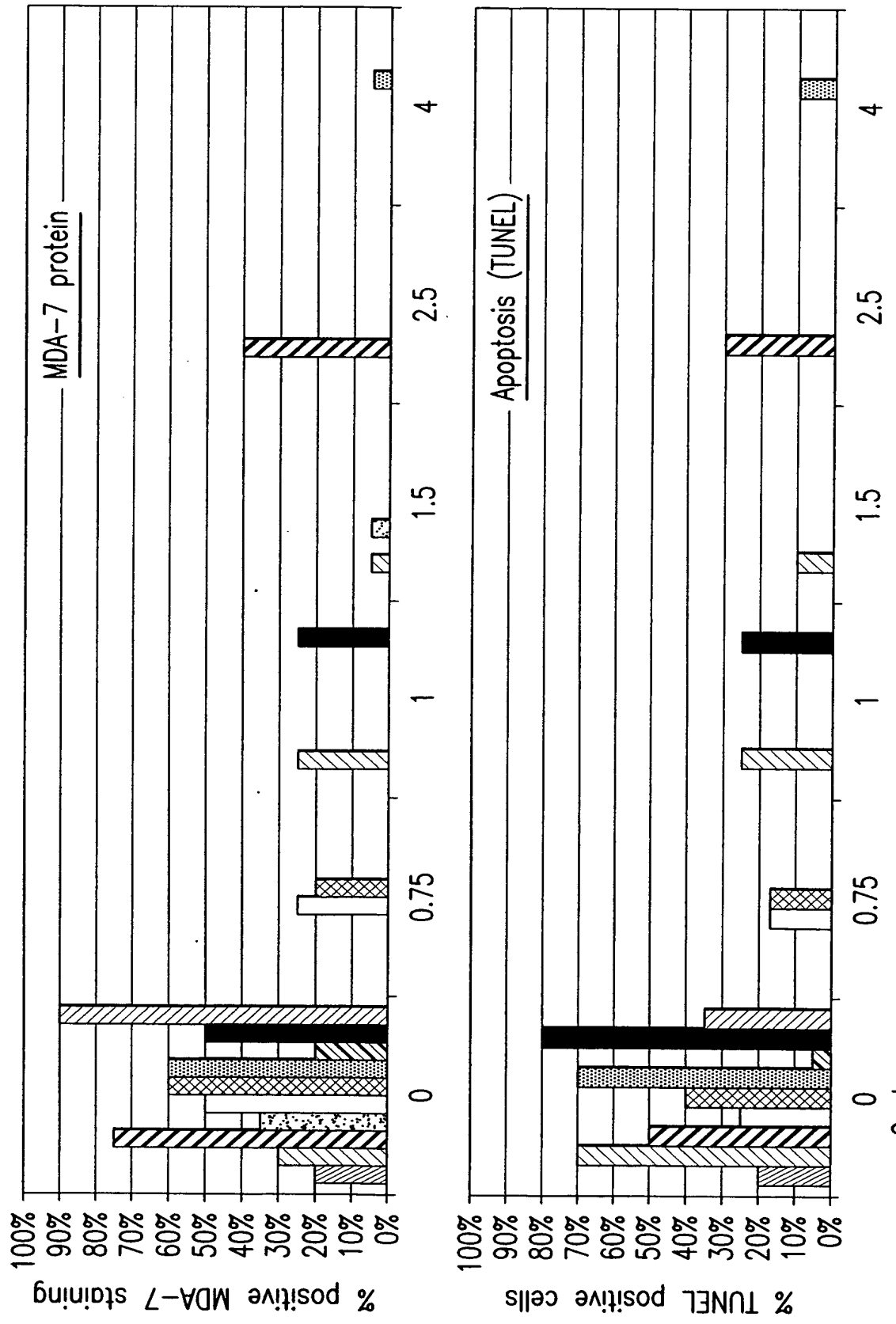

MDA-7 protein
Apoptosis (TUNEL)
% positive MDA-7 staining
% TUNEL positive cells
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
0.75
1
1.5
2.5
4
Center
Lesion radius (cm)

FIG.38

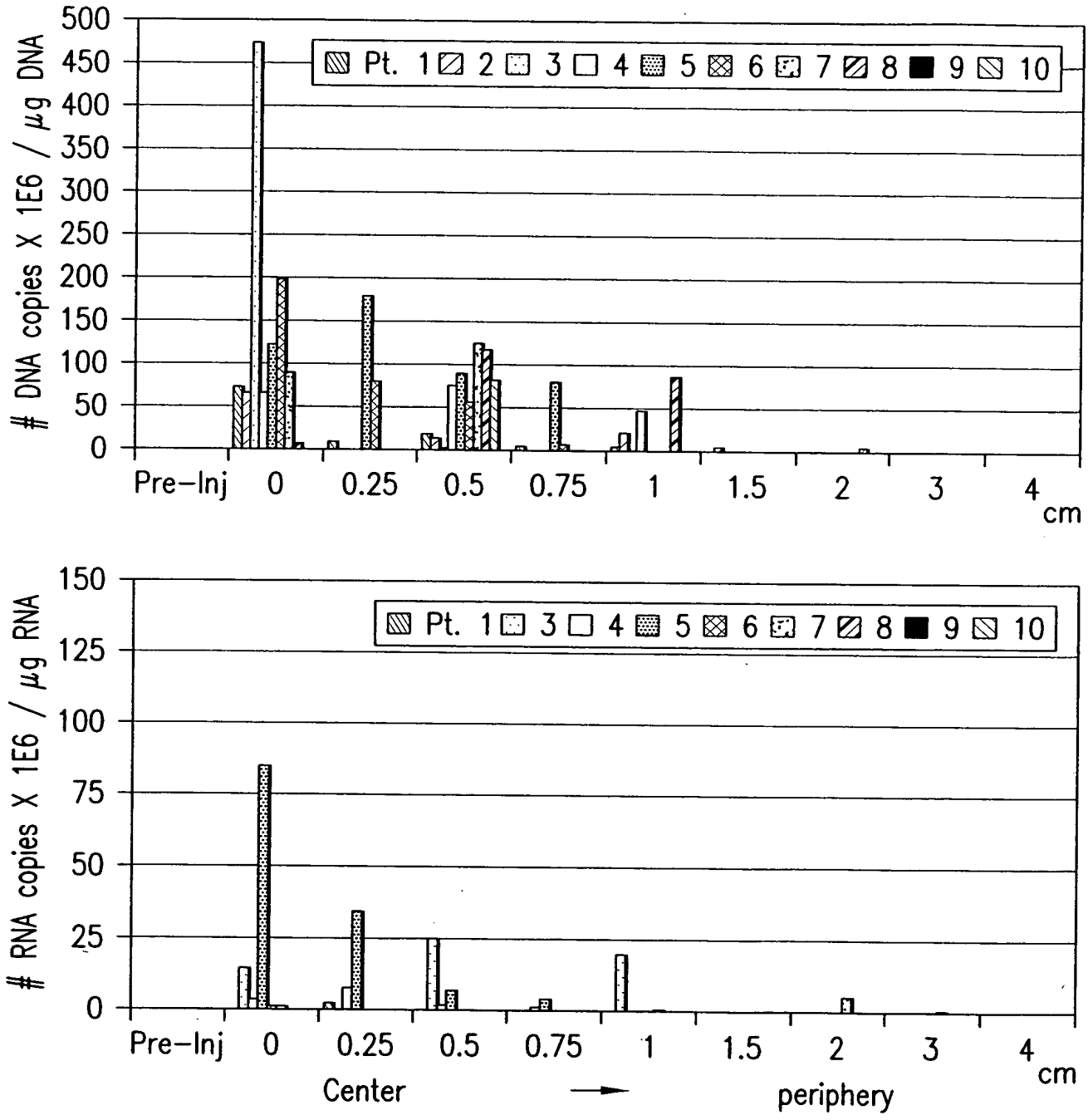

DNA copies X 1E6 / µg DNA
500
450
400
350
300
250
200
150
100
50
0
Pt. 1 2 3 4 5 6 7 8 9 10
Pre-Inj 0 0.25 0.5 0.75 1 1.5 2 3 4
cm
RNA copies X 1E6 / µg RNA
150
125
100
75
50
25
0
Pt. 1 3 4 5 6 7 8 9 10
Pre-Inj 0 0.25 0.5 0.75 1 1.5 2 3 4
cm
Center
periphery

FIG.39A

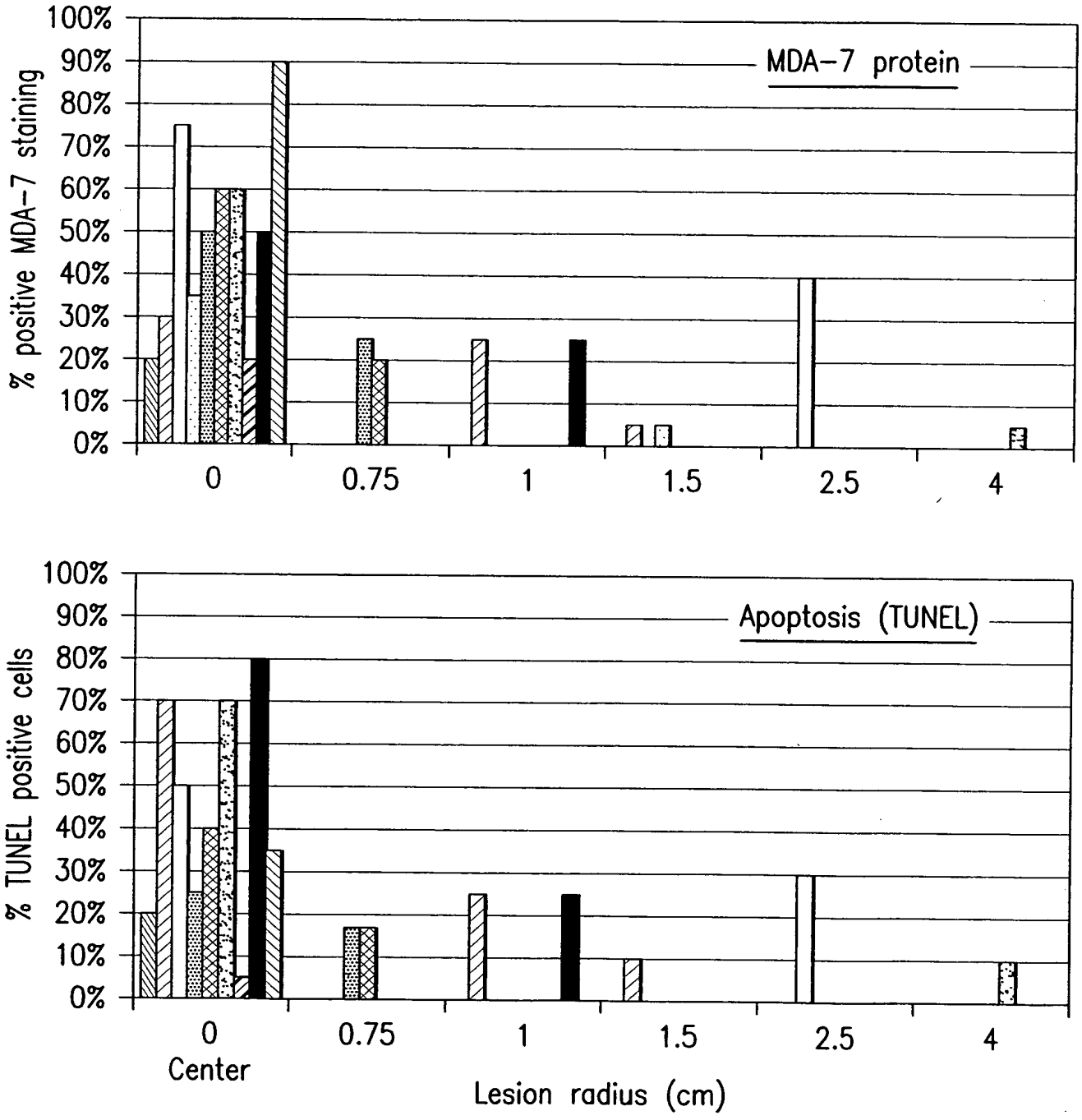

MDA-7 protein
% positive MDA-7 staining
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
0.75
1
1.5
2.5
4
Apoptosis (TUNEL)
% TUNEL positive cells
Center
Lesion radius (cm)

FIG.39B

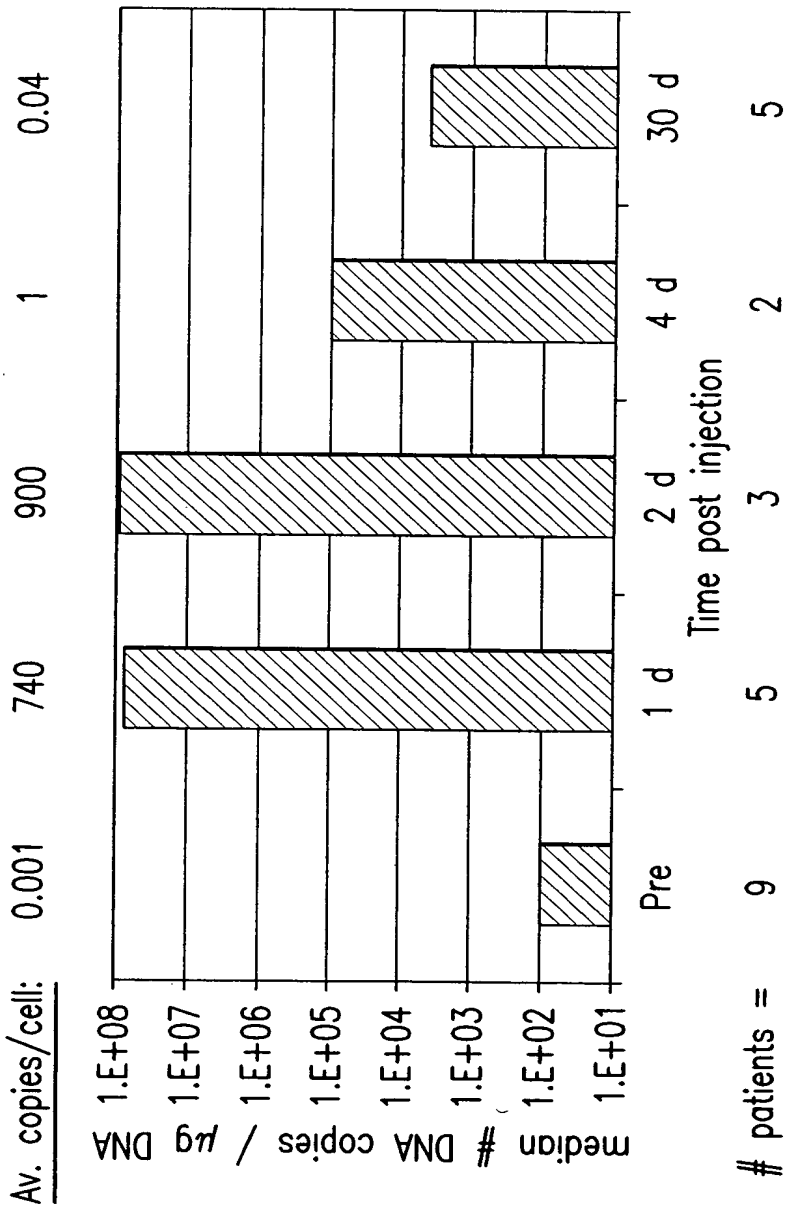

Av. copies/cell: 0.001 740 900 1 0.04
median # DNA copies / µg DNA
1.E+08
1.E+07
1.E+06
1.E+05
1.E+04
1.E+03
1.E+02
1.E+01
Pre
1 d
2 d
4 d
30 d
Time post injection
patients = 9 5 3 2 5

FIG.40

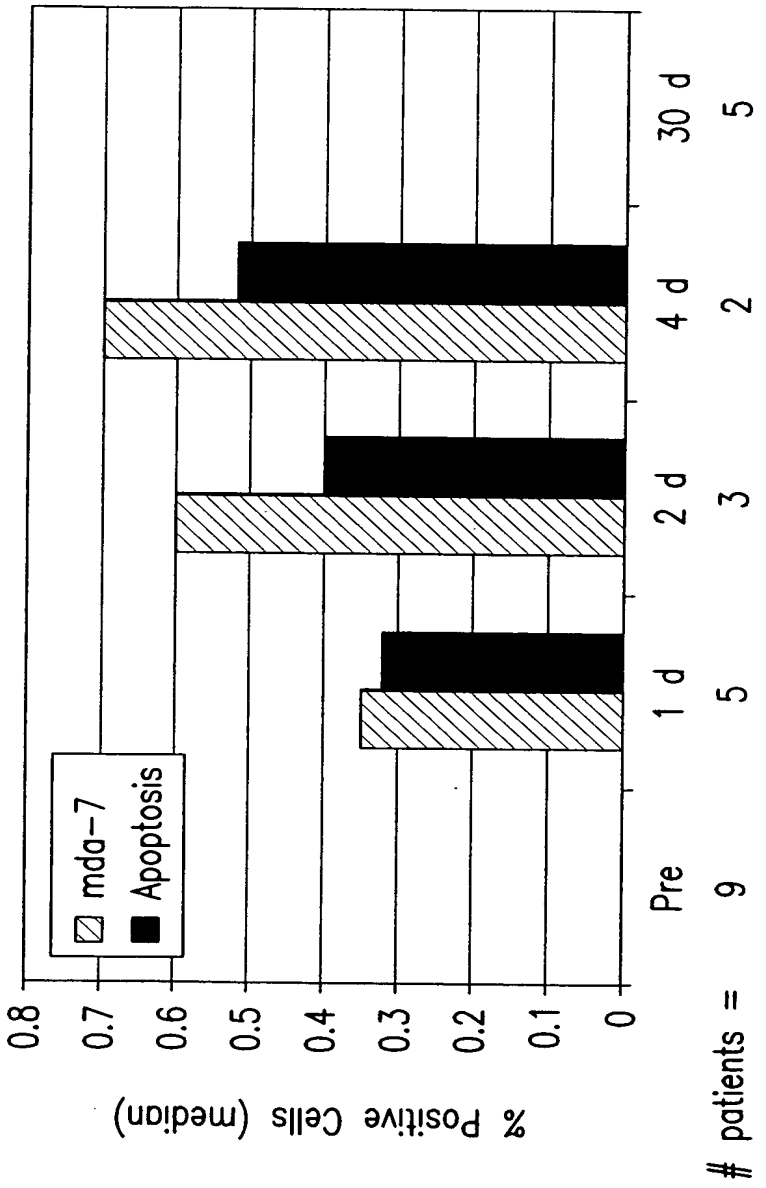

mda-7
Apoptosis
% Positive Cells (median)
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
patients =
9
5
3
2
5
Pre
1 d
2 d
4 d
30 d

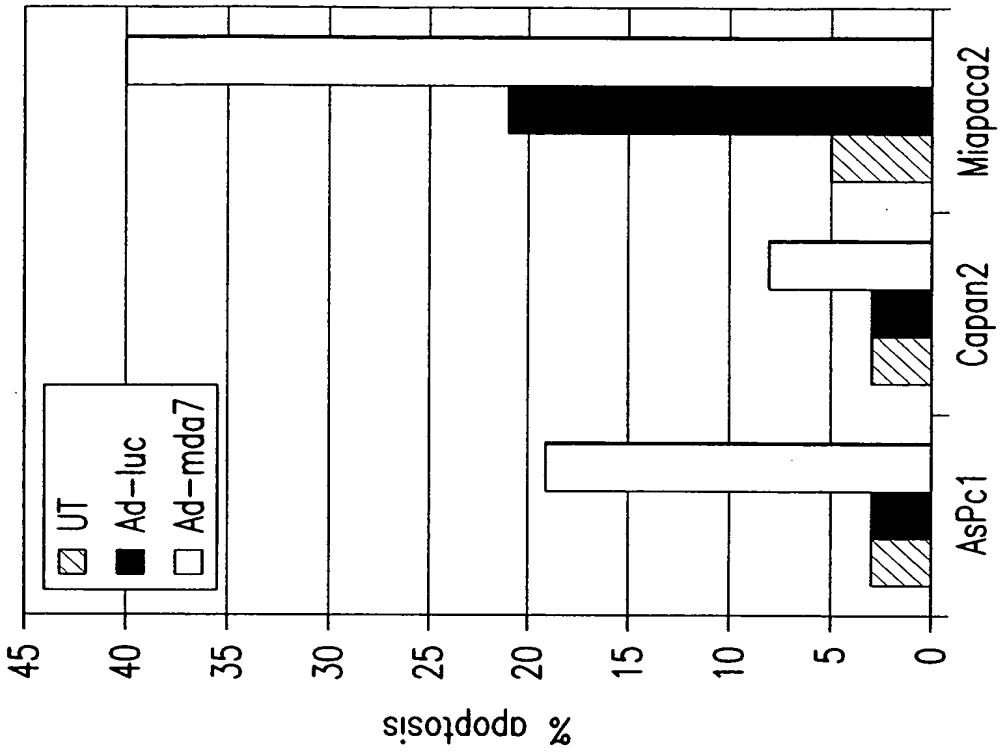
FIG.41

Single Dose (2E12 vp)			Clinical Activity (Y/N)		
Patient	Primary Histology	# injections	Local	Remote	Comment
71	Renal Cell Ca	1	N	N	Withdrew prior to day 30
72	TCC Bladder	1	N	N	
73	Melanoma	1	N	N	
74	Colo-Rectal	1	N	N	
75	SCCHN	1	N	N	Withdrew prior to day 30
76	SCCHN	1	N	N	
77	SCCHN	1	N	N	
Repeat Dose (2E12 vp biweekly x3)					
81	AdenoCa	3	–	–	Withdrew
83	Melanoma	12	Y*	Y**	CR
84	Melanoma	12	N	N	Stable Disease
85	SCCHN	6	Y	N	Central necrosis
86	NSCLC	3	–	–	Not eval
87	SCCHN	6	Y	pending	On study
88	Melanoma	6	Y	pending	On study

* Three lesions treated consecutively: pCR in 1st, clinCR in 2nd, regression in 3rd
**marked crythema around remote cutaneous lesion

FIG.42

Replacement Sheet


% apoptosis
45
40
35
30
25
20
15
10
5
0
UT
Ad-luc
Ad-mda7
AsPc1
Capan2
Miapaca2

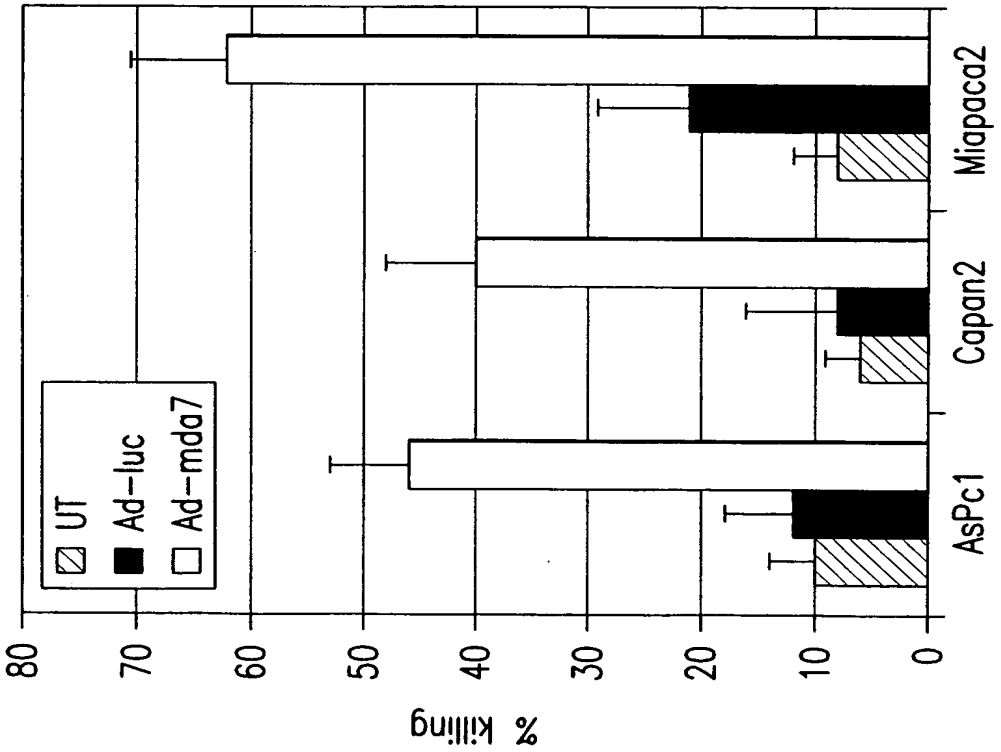

% killing
80
70
60
50
40
30
20
10
0
UT
Ad-luc
Ad-mda7
AsPc1
Capan2
Miapaca2

FIG.43

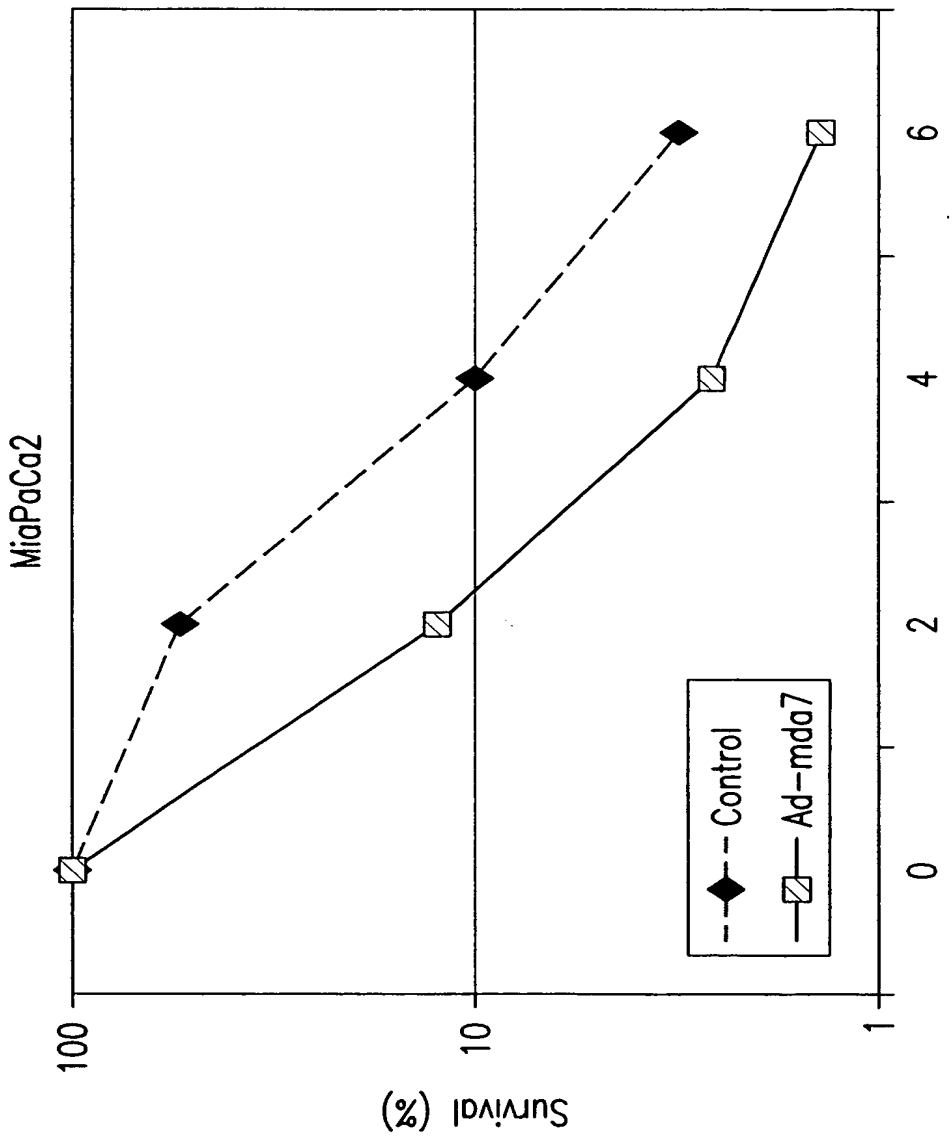


FIG.44

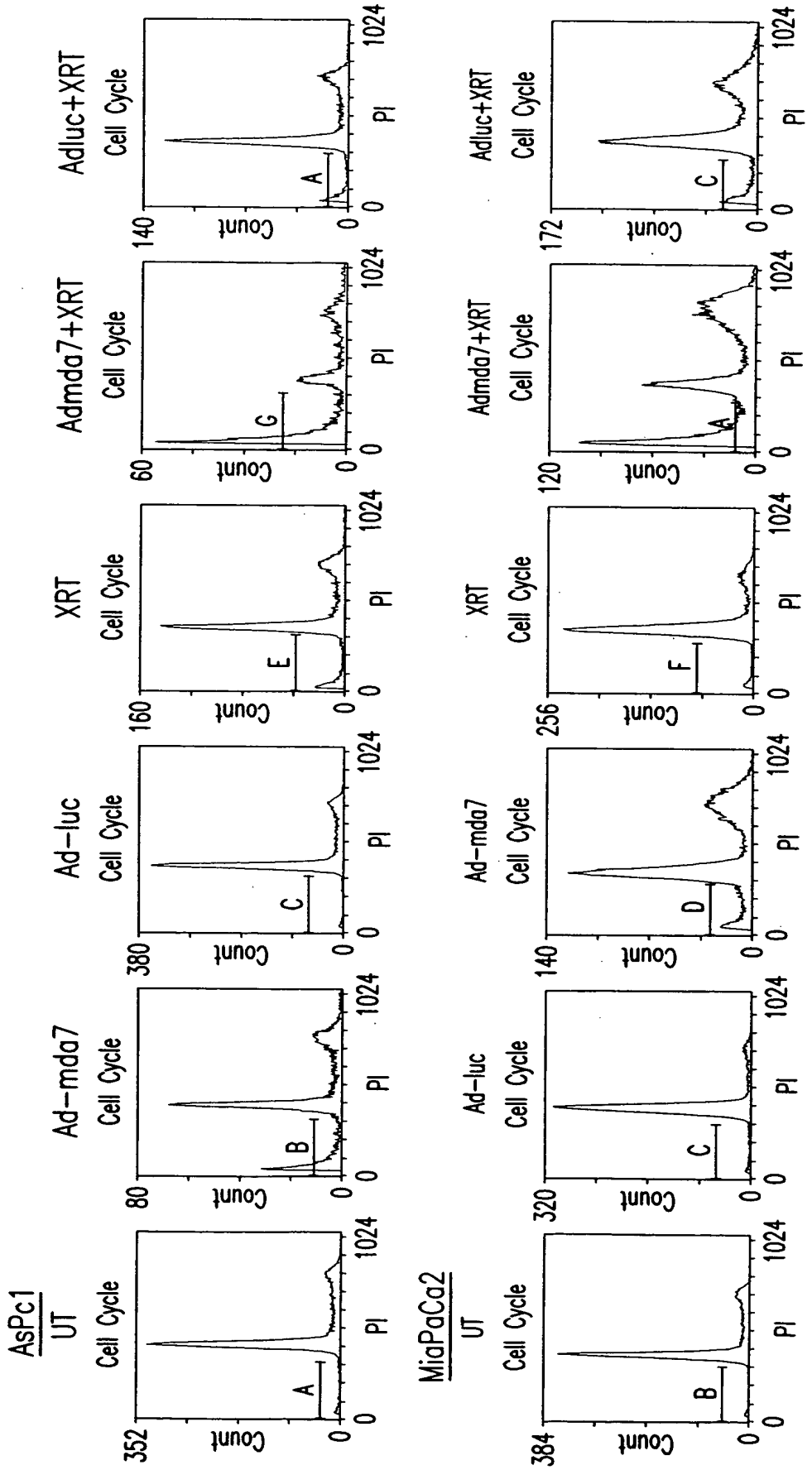

AsPc1
UT
Ad-mda7
Ad-luc
XRT
Admda7+XRT
Adluc+XRT
MiaPaCa2
UT
Ad-luc
Ad-mda7
XRT
Admda7+XRT
Adluc+XRT
Cell Cycle
Count
PI
0
1024
A
B
C
D
E
F
G
352
80
380
160
60
140
384
320
140
256
120
172

FIG.45

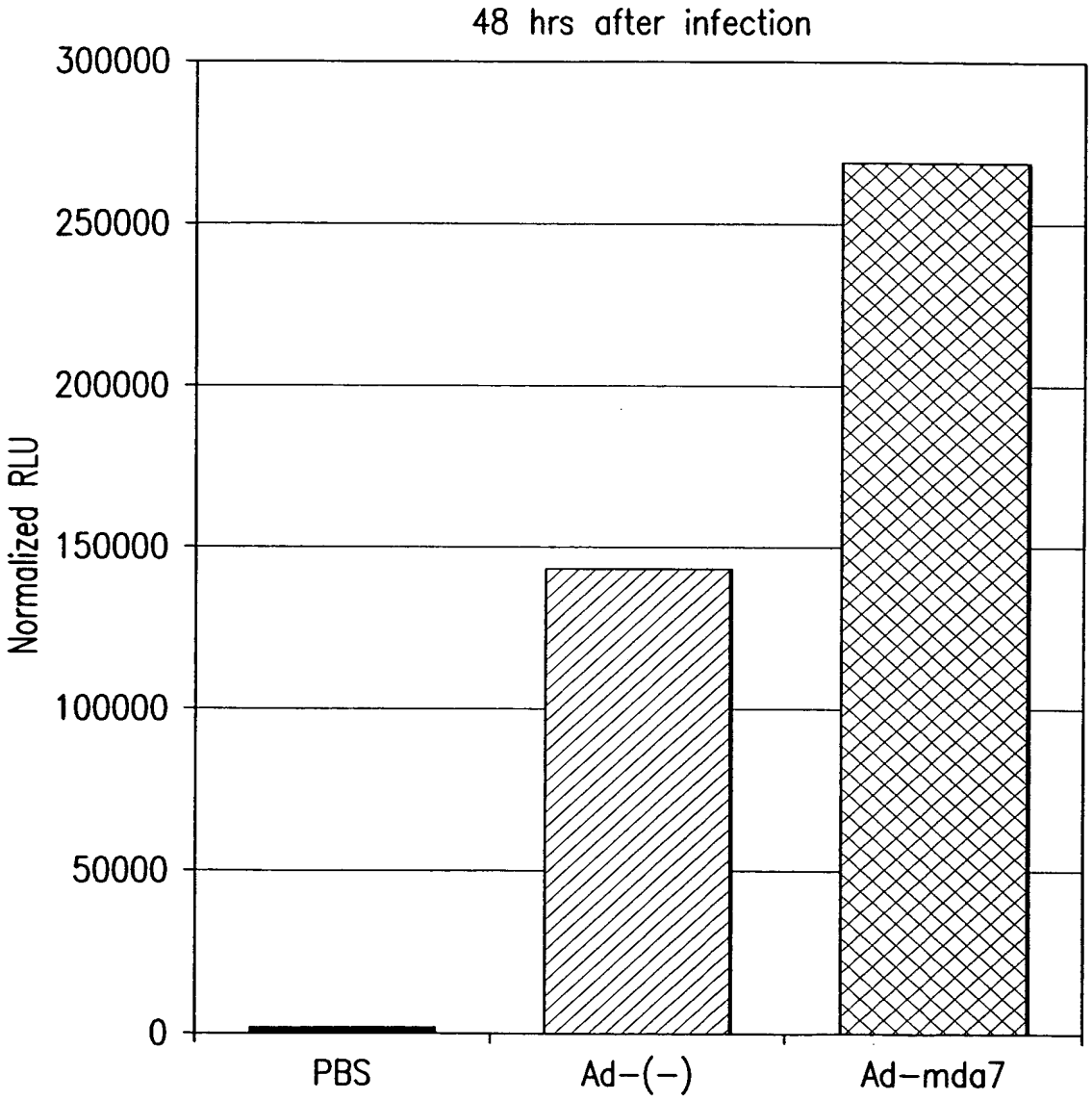
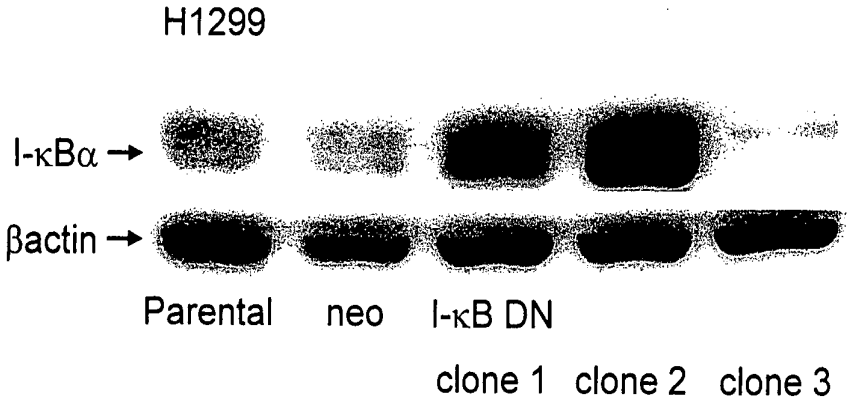

48 hrs after infection
300000
250000
200000
150000
100000
50000
0
Normalized RLU
PBS
Ad-(-)
Ad-mda7

FIG.46



IC 50 value

Ad-mda7

clone	(x10^{3}vp/cell)
neo	3.27 ± 1.1
clone1	2.58 ± 1.25
clone2	1.25 ± 0.3
clone3	3.98 ± 0.88

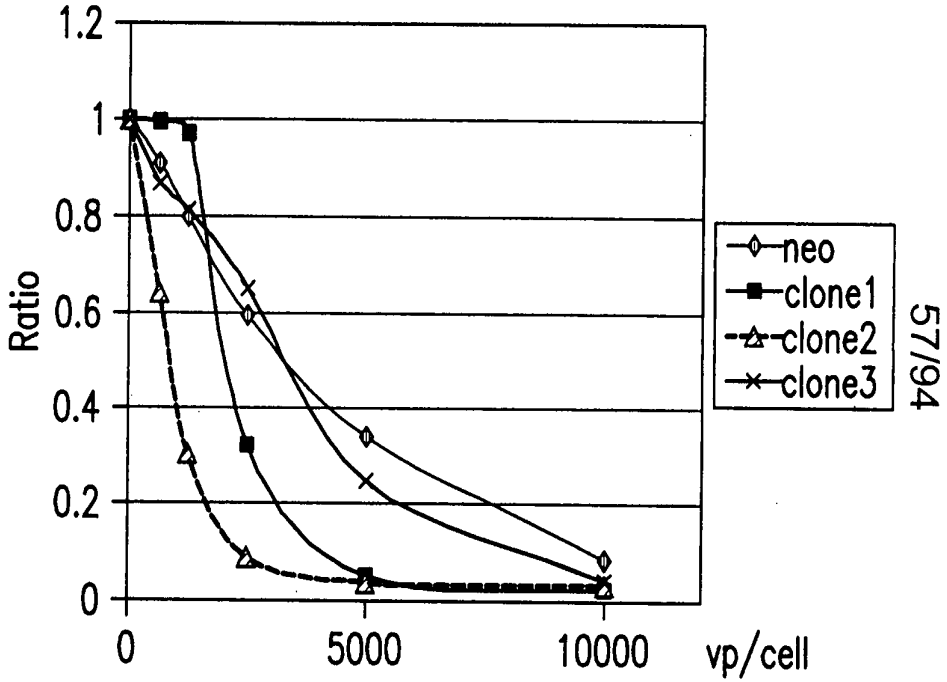
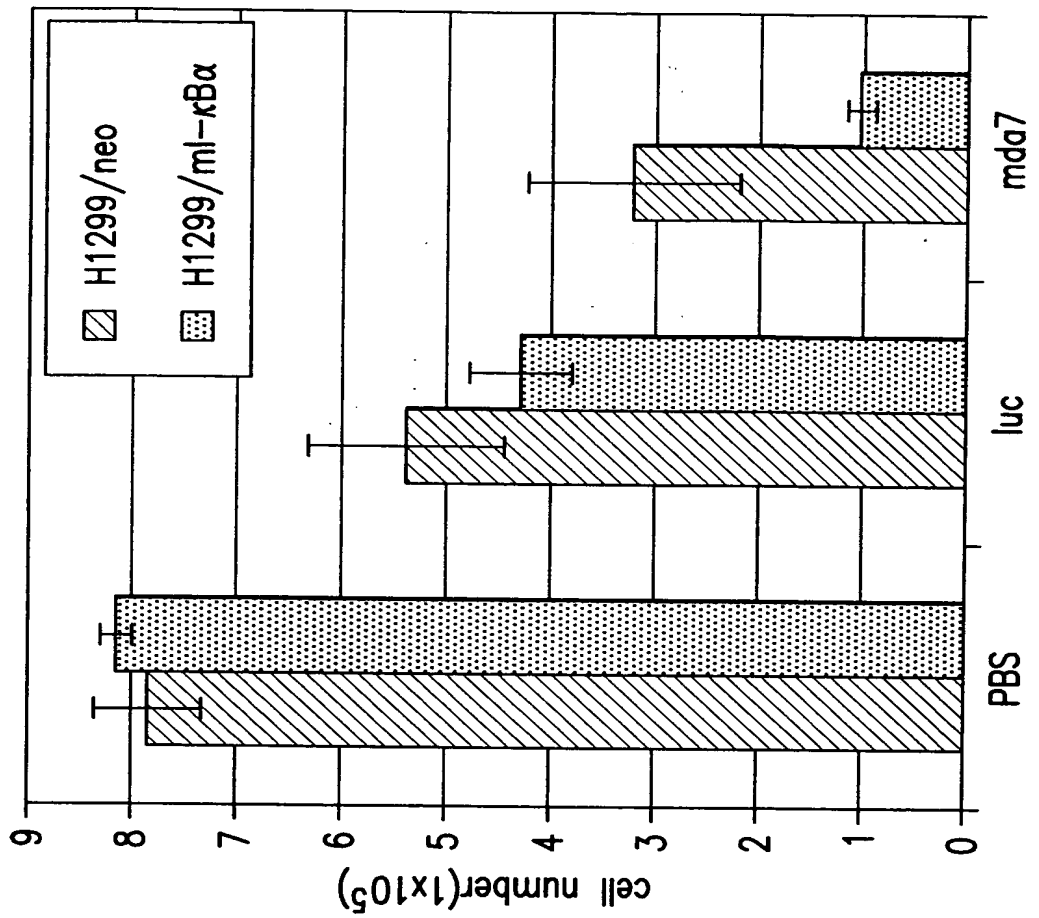


FIG.47

Replacement Sheet


H1299/neo
H1299/ml-κBα
cell number(1x10⁵)
0
1
2
3
4
5
6
7
8
9
PBS
luc
mda7

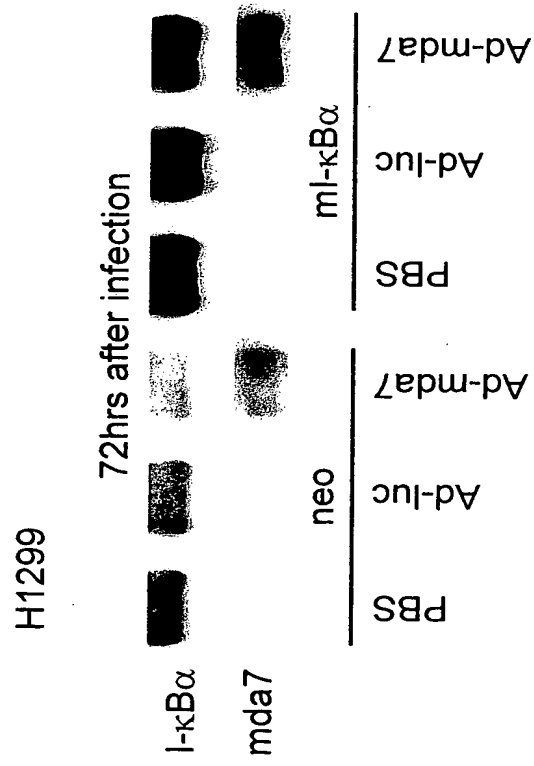

H1299
72hrs after infection
I-κBα
mda7
PBS
Ad-luc
Ad-mda7
neo
PBS
Ad-luc
Ad-mda7
ml-κBα

FIG.48

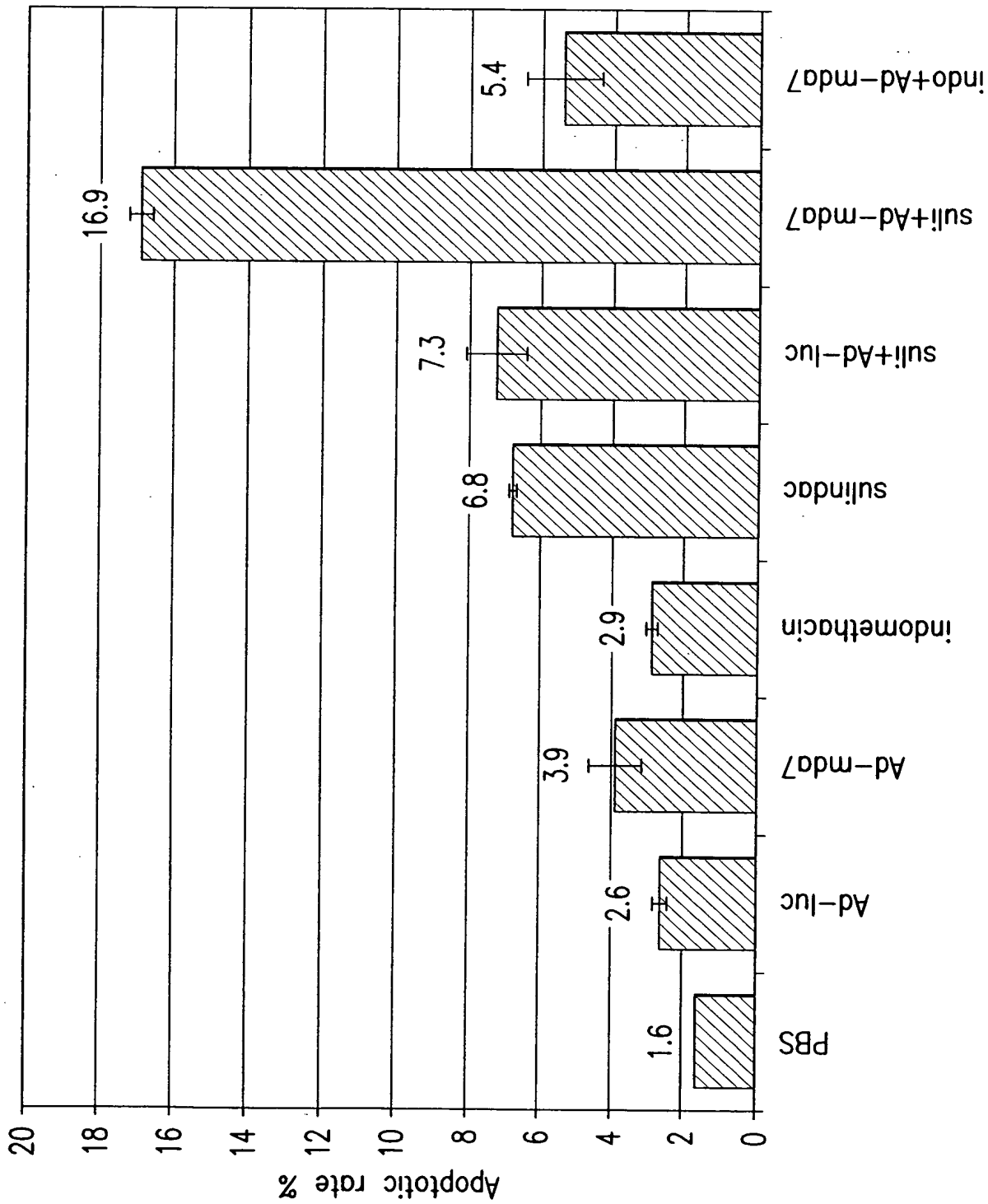
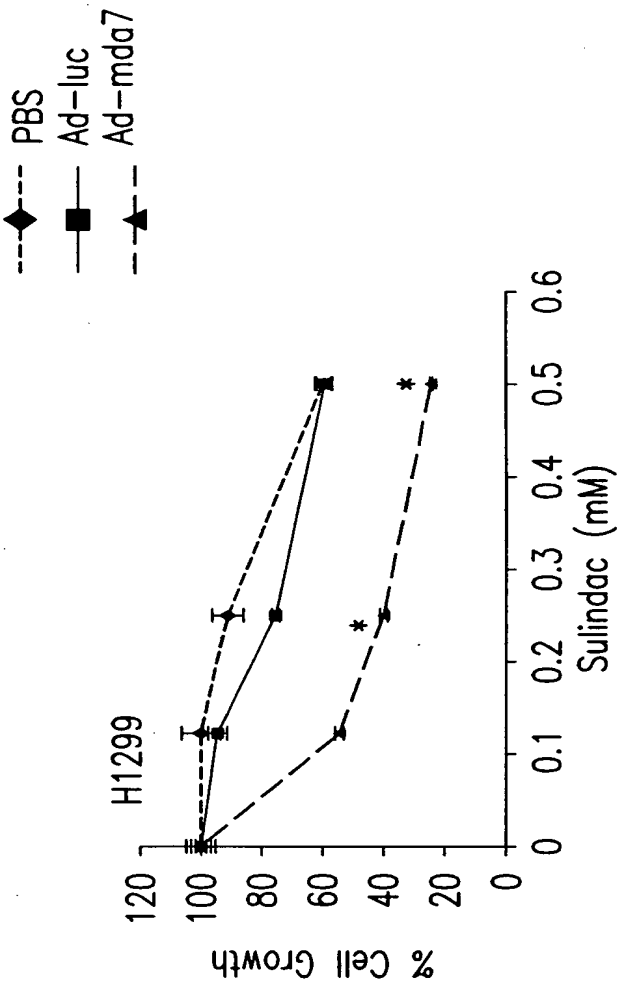
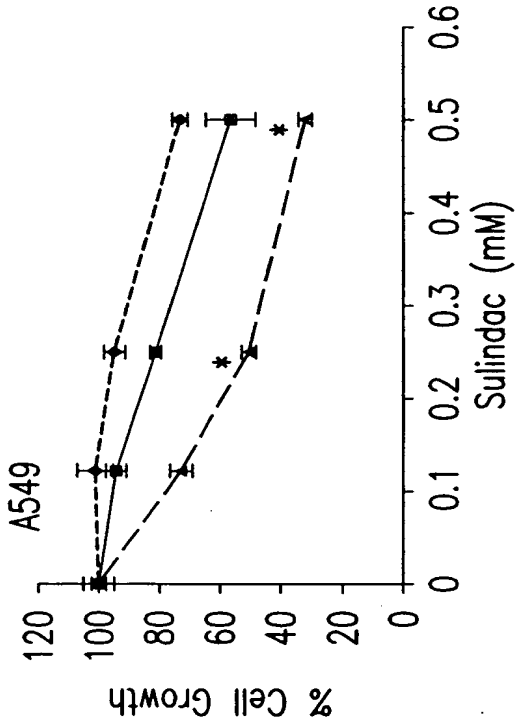

Apoptotic rate %
0
2
4
6
8
10
12
14
16
18
20
PBS
Ad-luc
Ad-mda7
indomethacin
sulindac
suli+Ad-luc
suli+Ad-mda7
indo+Ad-mda7
1.6
2.6
3.9
2.9
6.8
7.3
16.9
5.4

FIG.49A


PBS
Ad-luc
Ad-mda7
H1299
% Cell Growth
Sulindac (mM)
0
20
40
60
80
100
120
0.1
0.2
0.3
0.4
0.5
0.6
*


A549
% Cell Growth
Sulindac (mM)
0
20
40
60
80
100
120
0.1
0.2
0.3
0.4
0.5
0.6
*

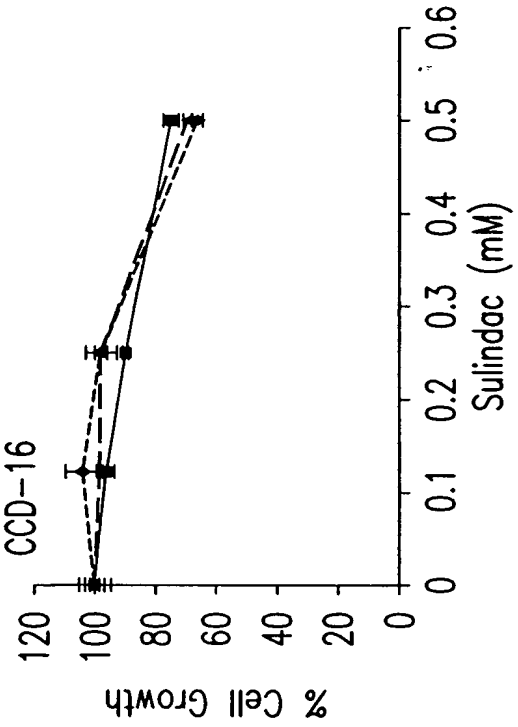

CCD-16
% Cell Growth
Sulindac (mM)
0
20
40
60
80
100
120
0.1
0.2
0.3
0.4
0.5
0.6

FIG.49B

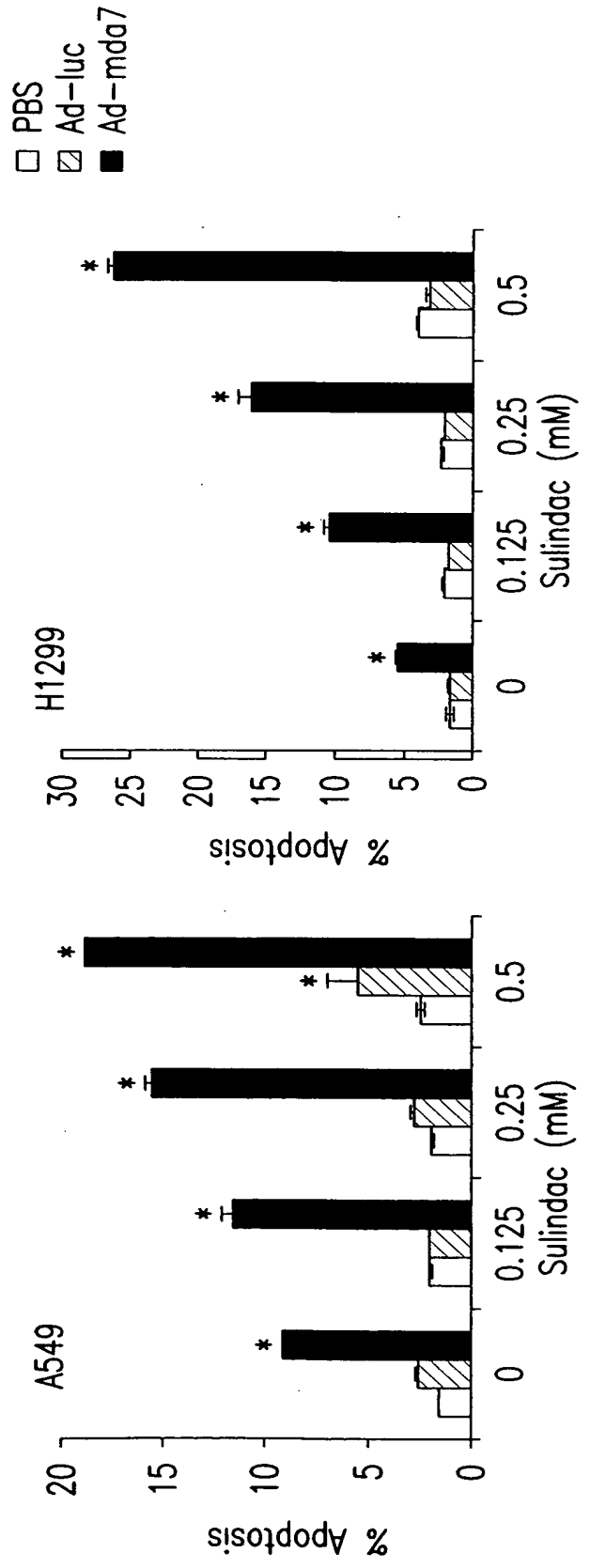

PBS
Ad-luc
Ad-mda7
H1299
A549
CCD16
% Apoptosis
Sulindac (mM)
0
0.125
0.25
0.5
*

FIG.49C

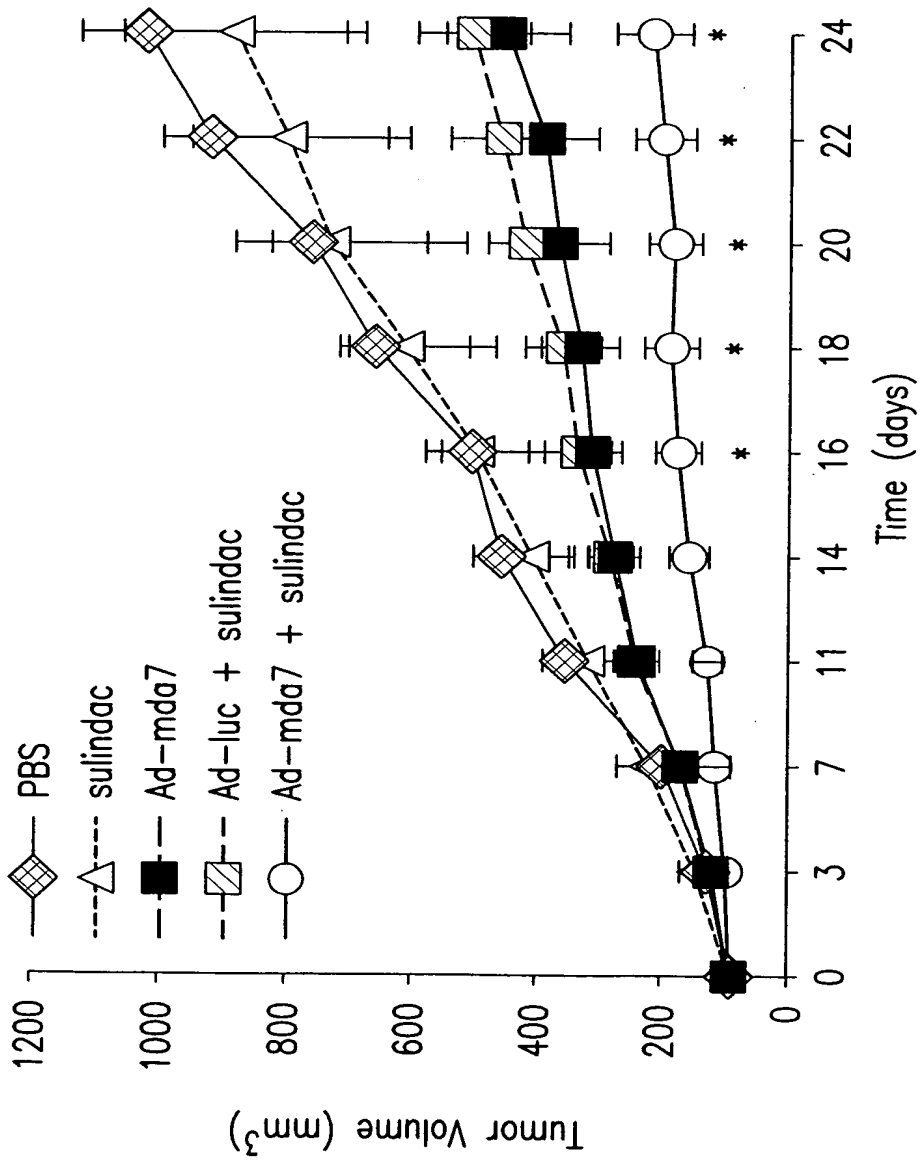

PBS
sulindac
Ad-mda7
Ad-luc + sulindac
Ad-mda7 + sulindac
Tumor Volume (mm3)
1200
1000
800
600
400
200
0
0
3
7
11
14
16
18
20
22
24
Time (days)
*
*
*
*
*

FIG.49D

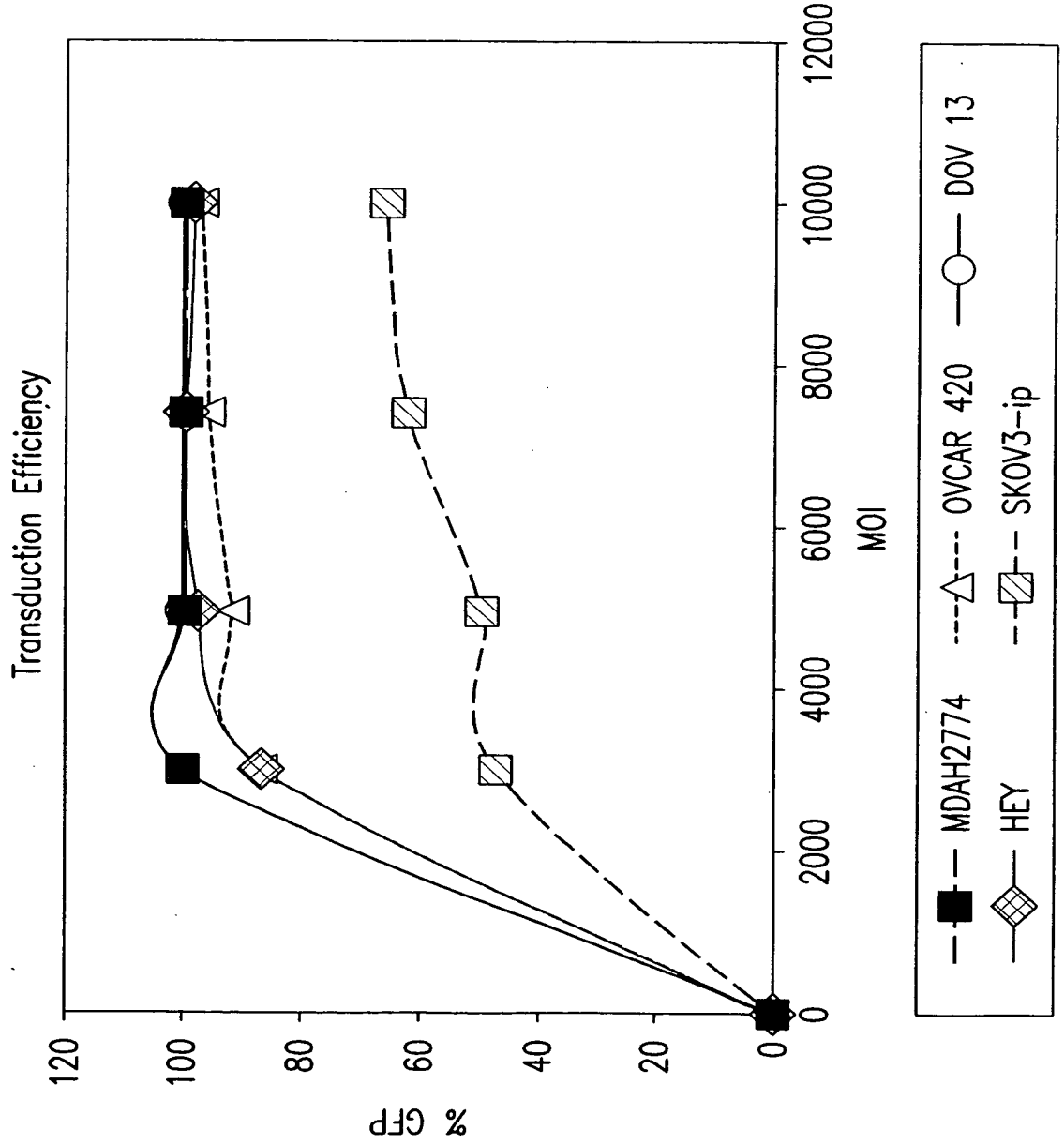
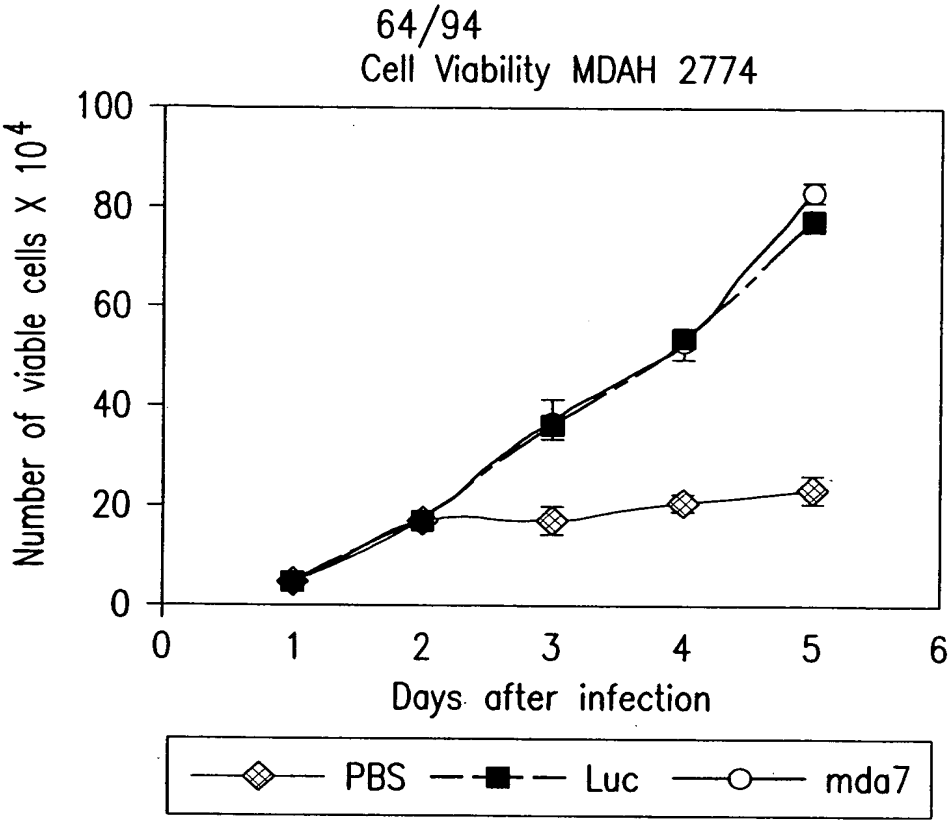

Transduction Efficiency
% GFP
MOI
0
20
40
60
80
100
120
2000
4000
6000
8000
10000
12000
MDAH2774
OVCAR 420
DOV 13
HEY
SKOV3-ip

FIG.50


Cell Viability MDAH 2774
Number of viable cells X 10^4
100
80
60
40
20
0
0
1
2
3
4
5
6
Days after infection
PBS
Luc
mda7

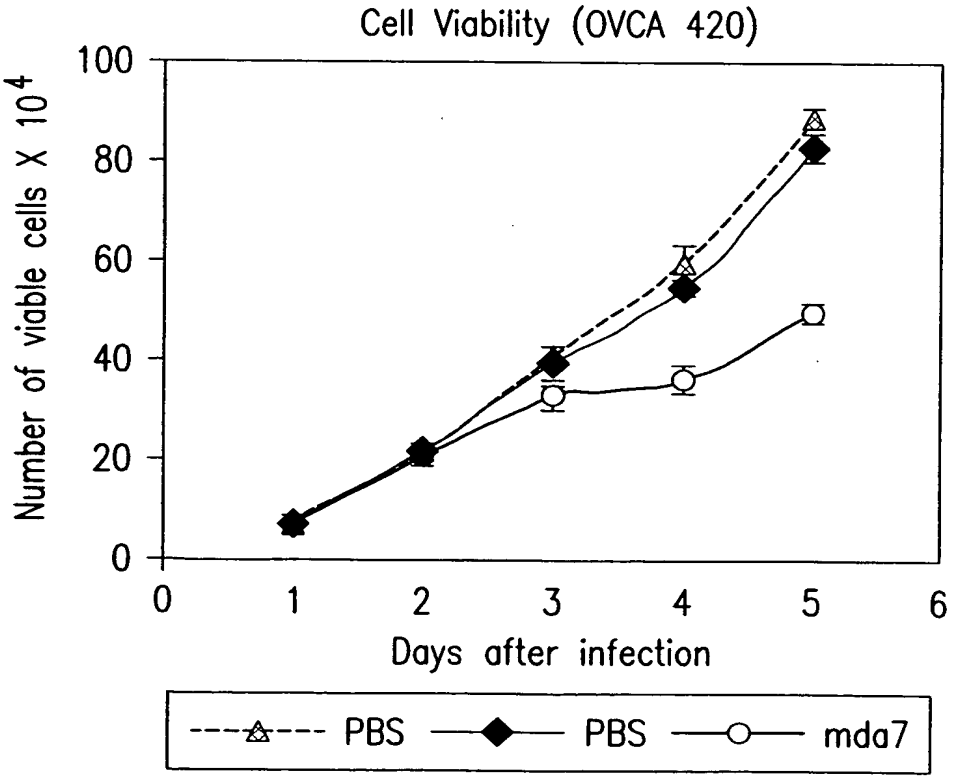

Cell Viability (OVCA 420)
Number of viable cells X 10^4
100
80
60
40
20
0
0
1
2
3
4
5
6
Days after infection
PBS
PBS
mda7

FIG.51

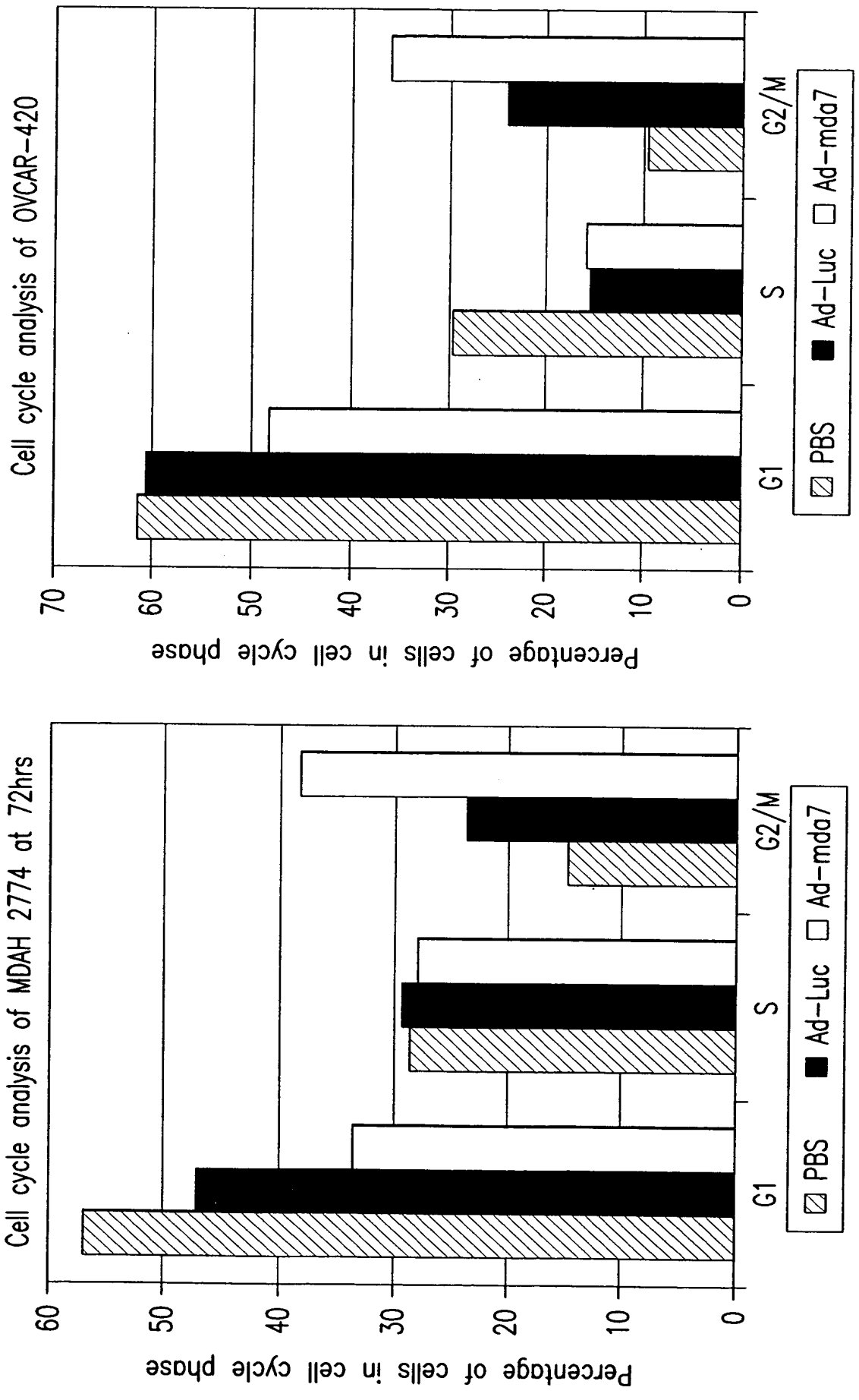

Cell cycle analysis of OVCAR-420
Percentage of cells in cell cycle phase
0
10
20
30
40
50
60
70
G1
S
G2/M
PBS
Ad-Luc
Ad-mda7
Cell cycle analysis of MDAH 2774 at 72hrs
Percentage of cells in cell cycle phase
0
10
20
30
40
50
60
G1
S
G2/M
PBS
Ad-Luc
Ad-mda7

FIG.52

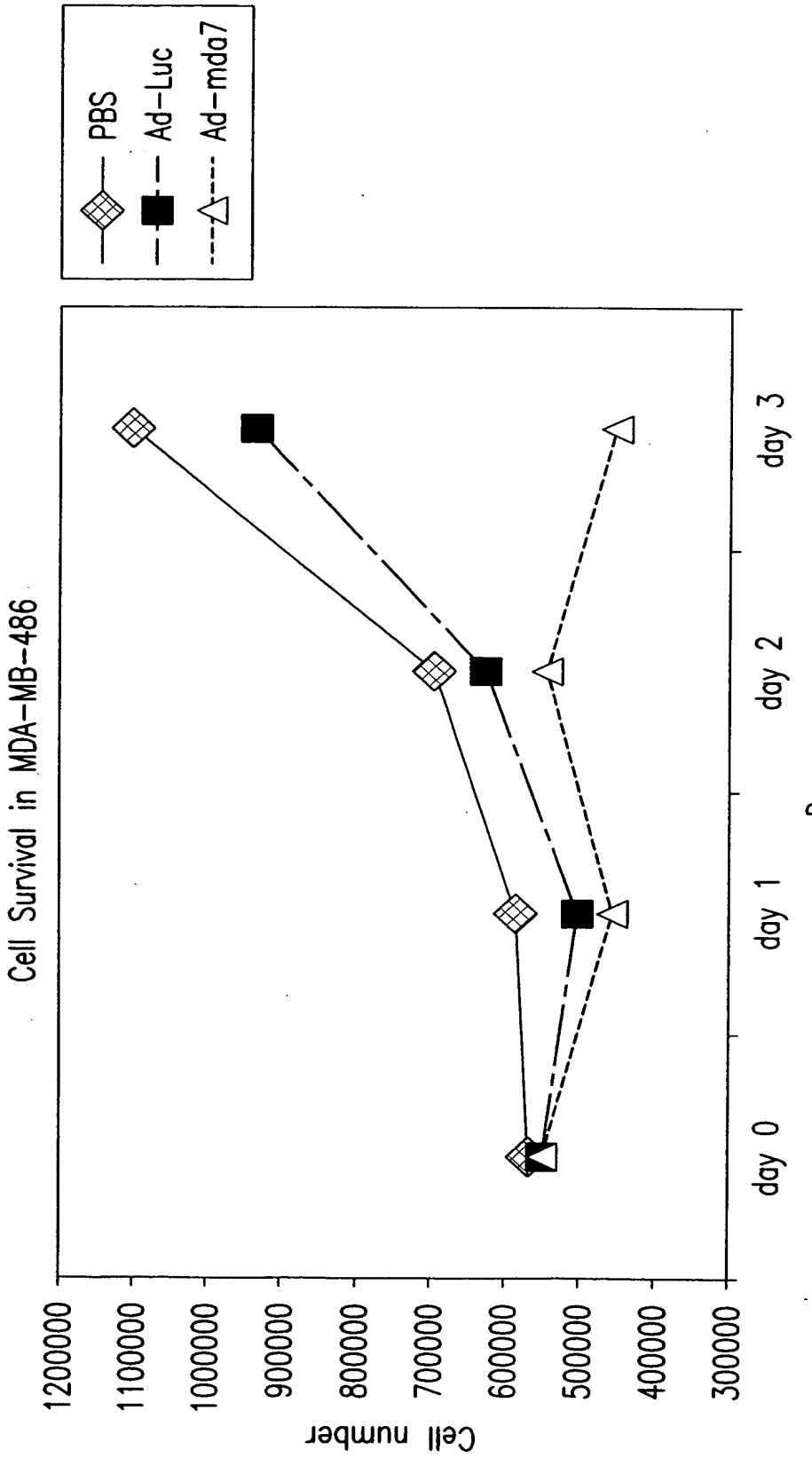

Cell Survival in MDA-MB-486
PBS
Ad-Luc
Ad-mda7
Cell number
1200000
1100000
1000000
900000
800000
700000
600000
500000
400000
300000
day 0
day 1
day 2
day 3
Day

FIG.53

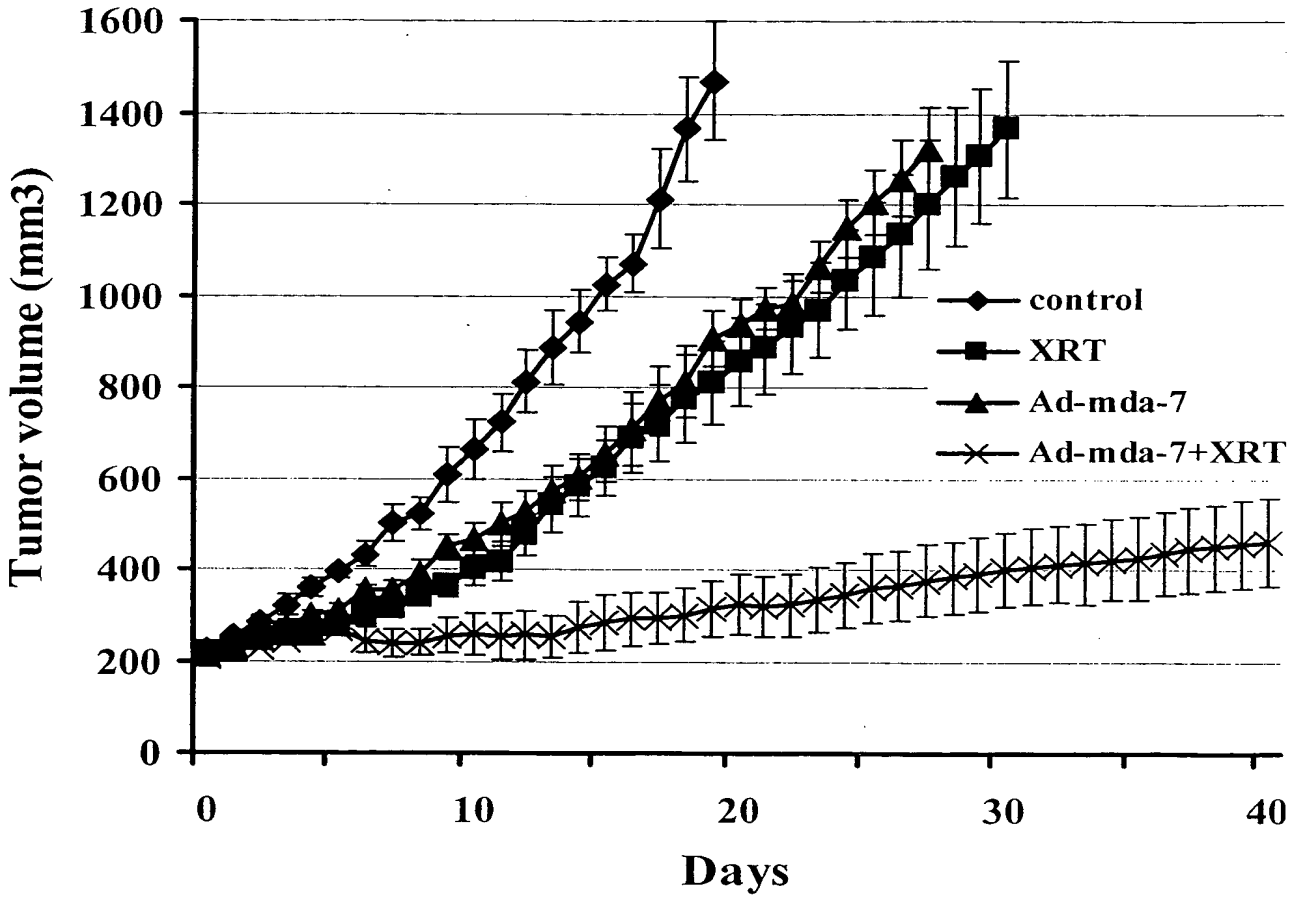

1600
1400
1200
1000
800
600
400
200
0
Tumor volume (mm3)
0
10
20
30
40
Days
control
XRT
Ad-mda-7
Ad-mda-7+XRT

FIG.54A

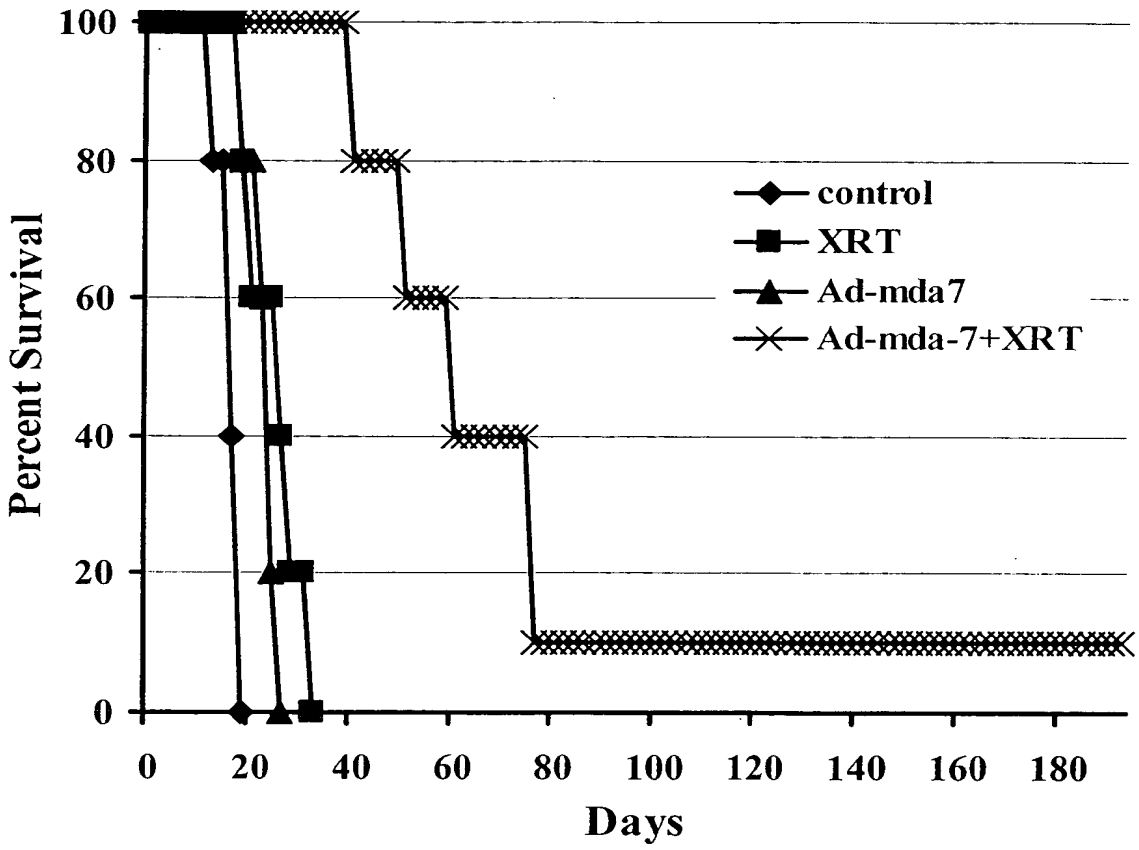

100
80
60
40
20
0
Percent Survival
0
20
40
60
80
100
120
140
160
180
Days
control
XRT
Ad-mda7
Ad-mda-7+XRT

FIG.54B

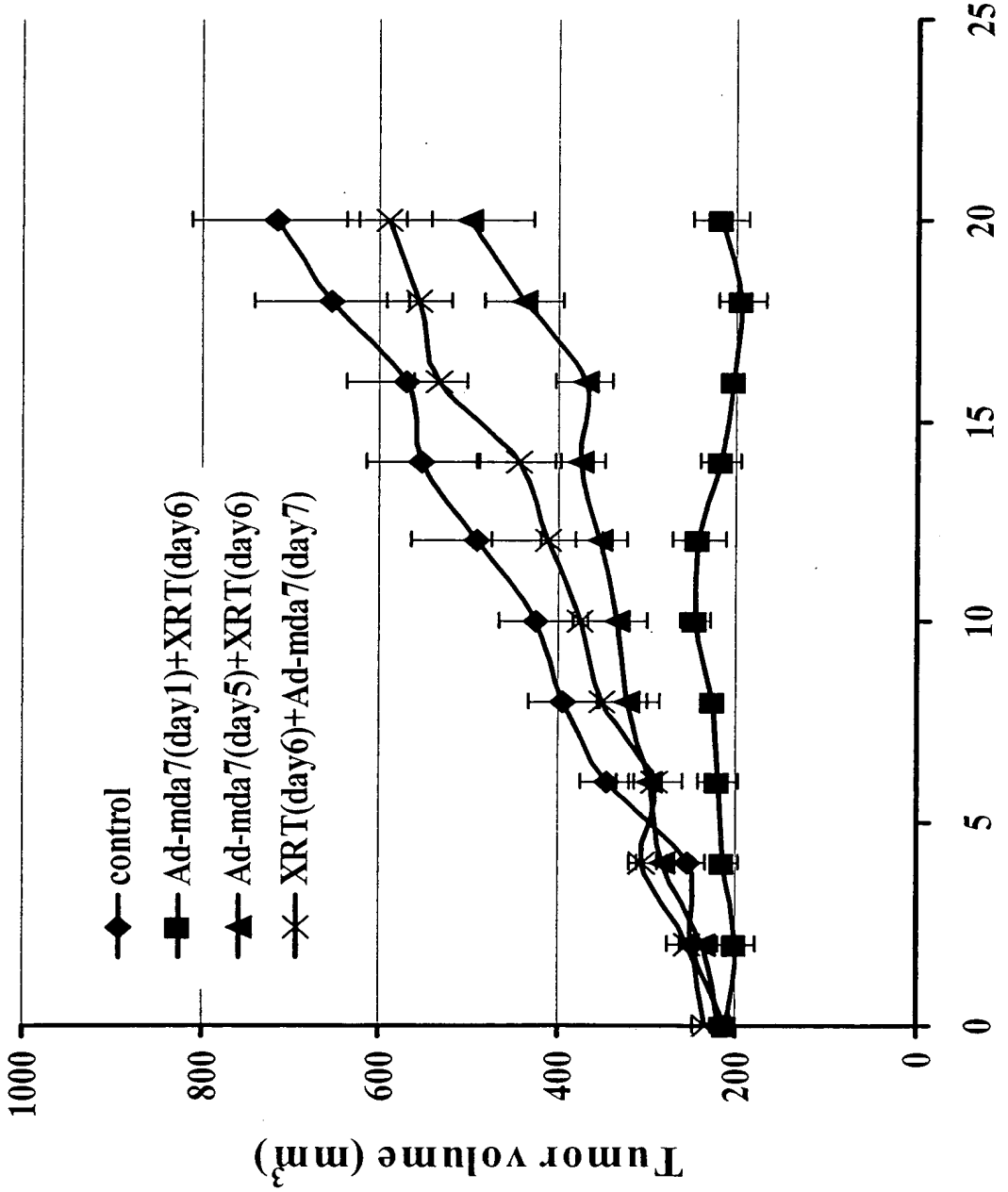

Tumor volume (mm³)
1000
800
600
400
200
0
0
5
10
15
20
25
Days
control
Ad-mda7(day1)+XRT(day6)
Ad-mda7(day5)+XRT(day6)
XRT(day6)+Ad-mda7(day7)

FIG.55

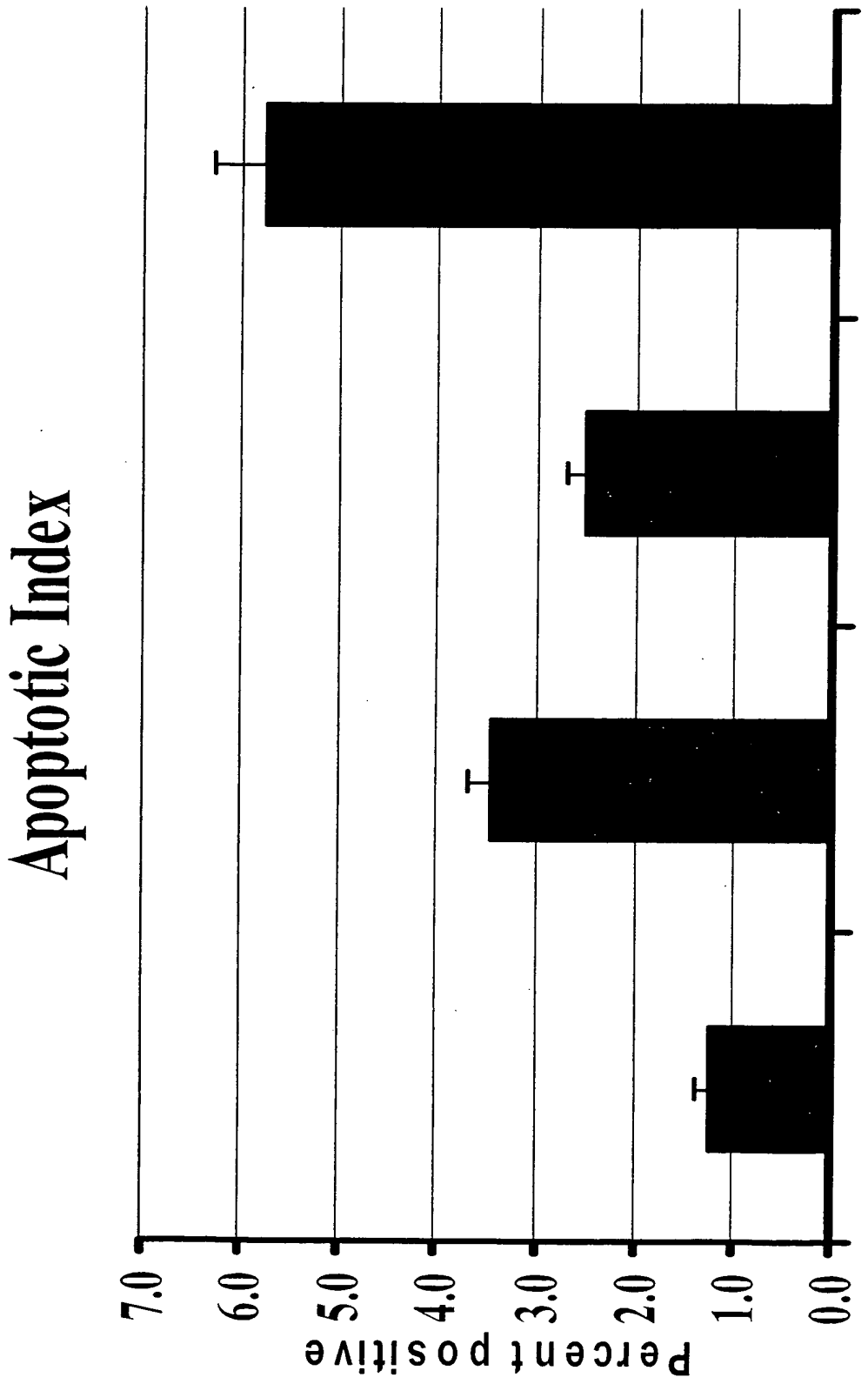

Apoptotic Index
Percent positive
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
control
XRT
Ad-mda7
Ad-mda7+XRT

FIG.56

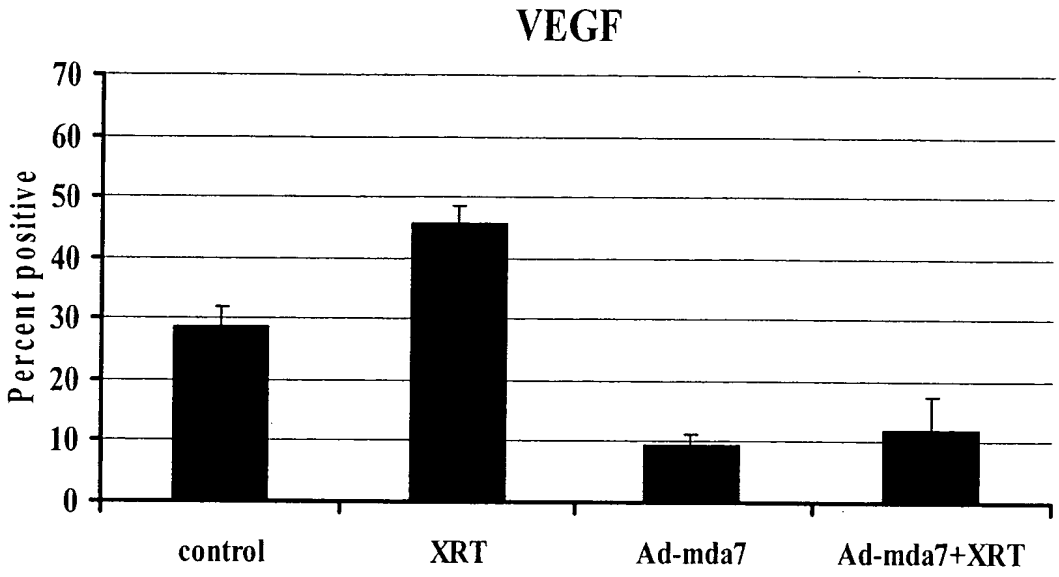


FIG.57A

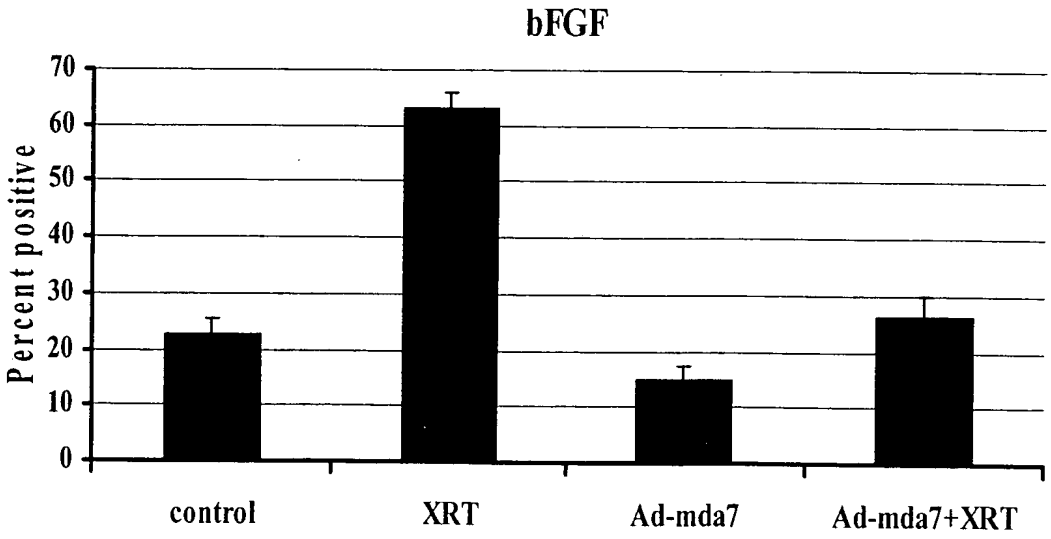


FIG.57B

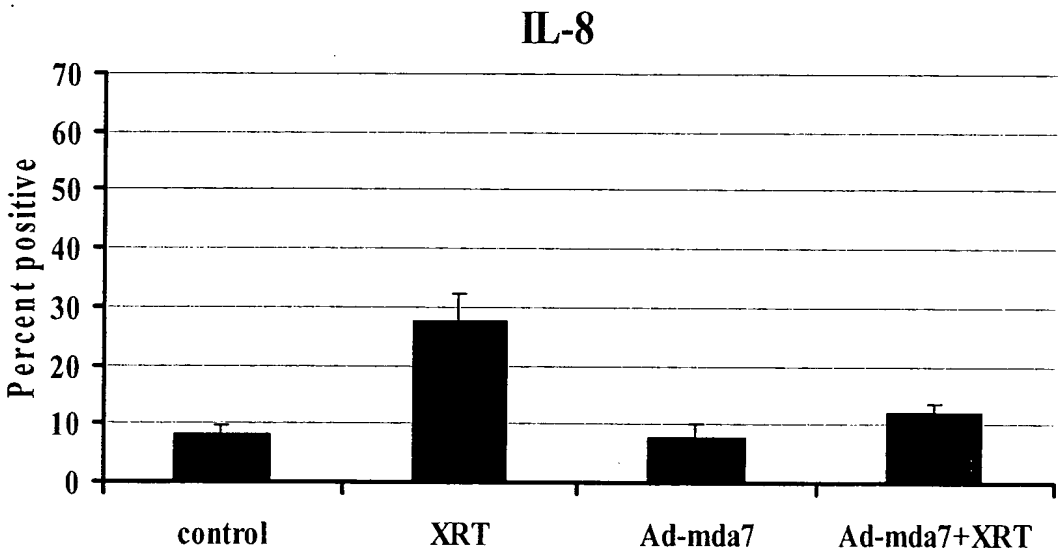

IL-8
Percent positive
70
60
50
40
30
20
10
0
control
XRT
Ad-mda7
Ad-mda7+XRT

FIG.57C

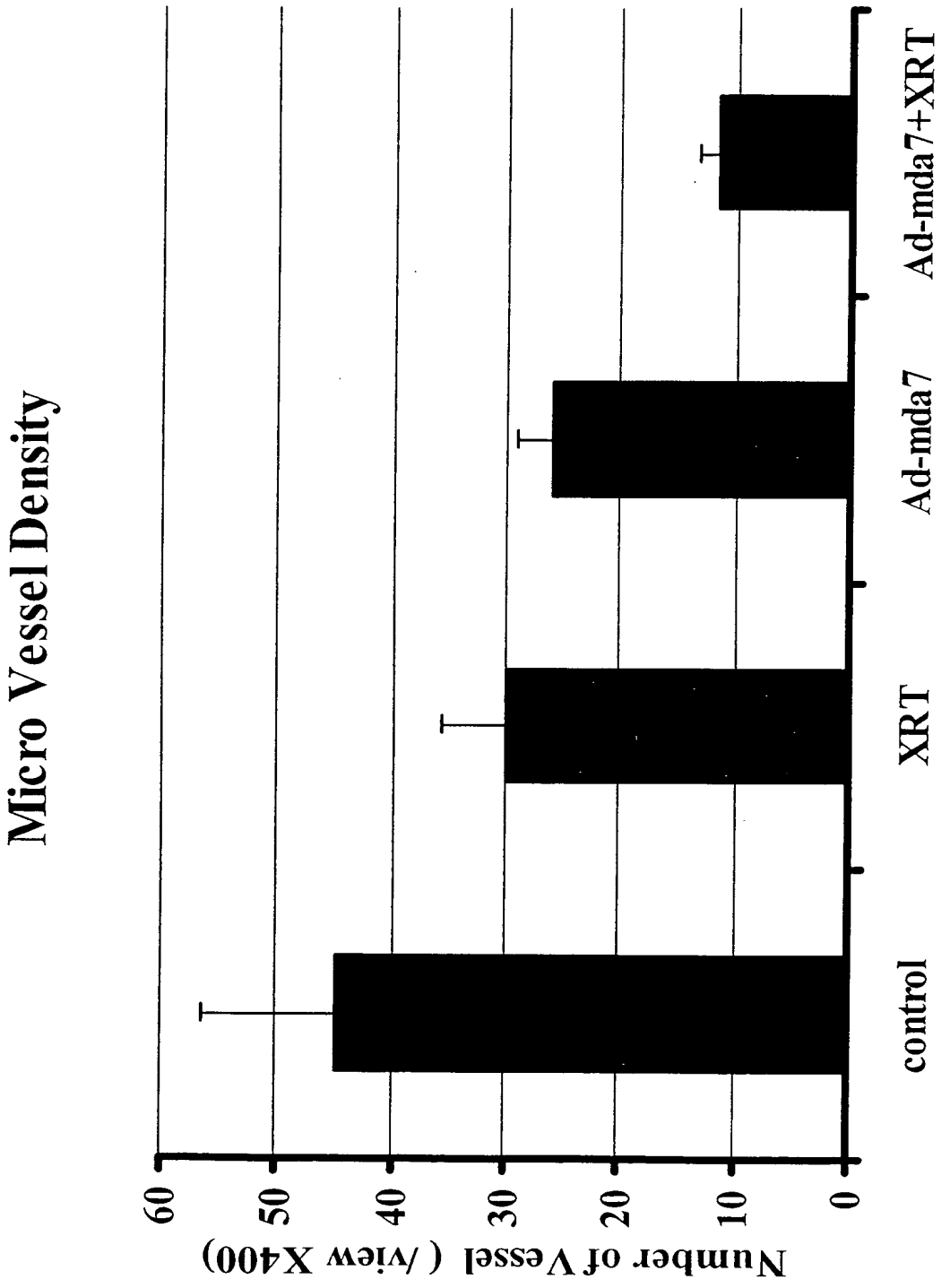

Micro Vessel Density
Number of Vessel (/view X400)
60
50
40
30
20
10
0
control
XRT
Ad-mda7
Ad-mda7+XRT

FIG.58

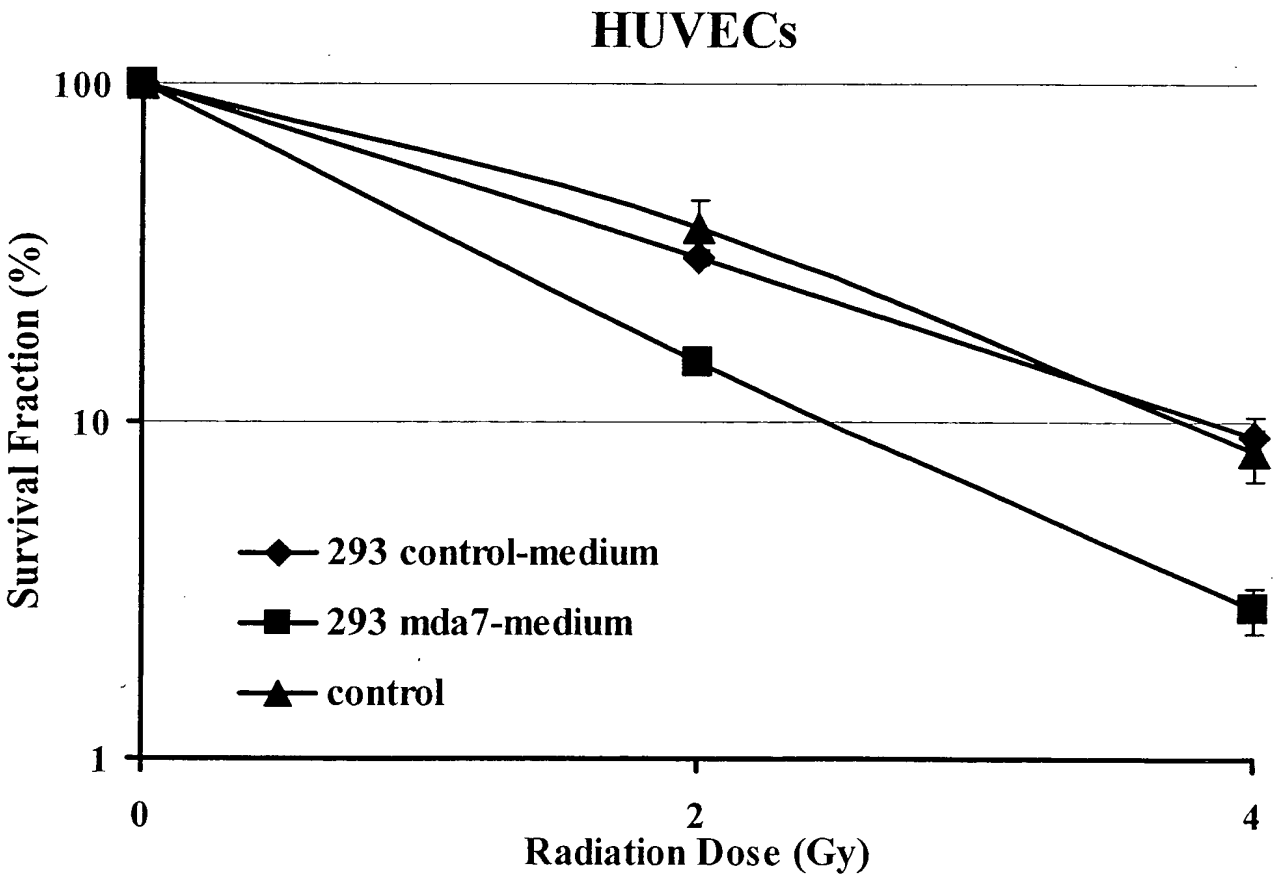

HUVECs
100
10
1
Survival Fraction (%)
293 control-medium
293 mda7-medium
control
0
2
4
Radiation Dose (Gy)

FIG.59A

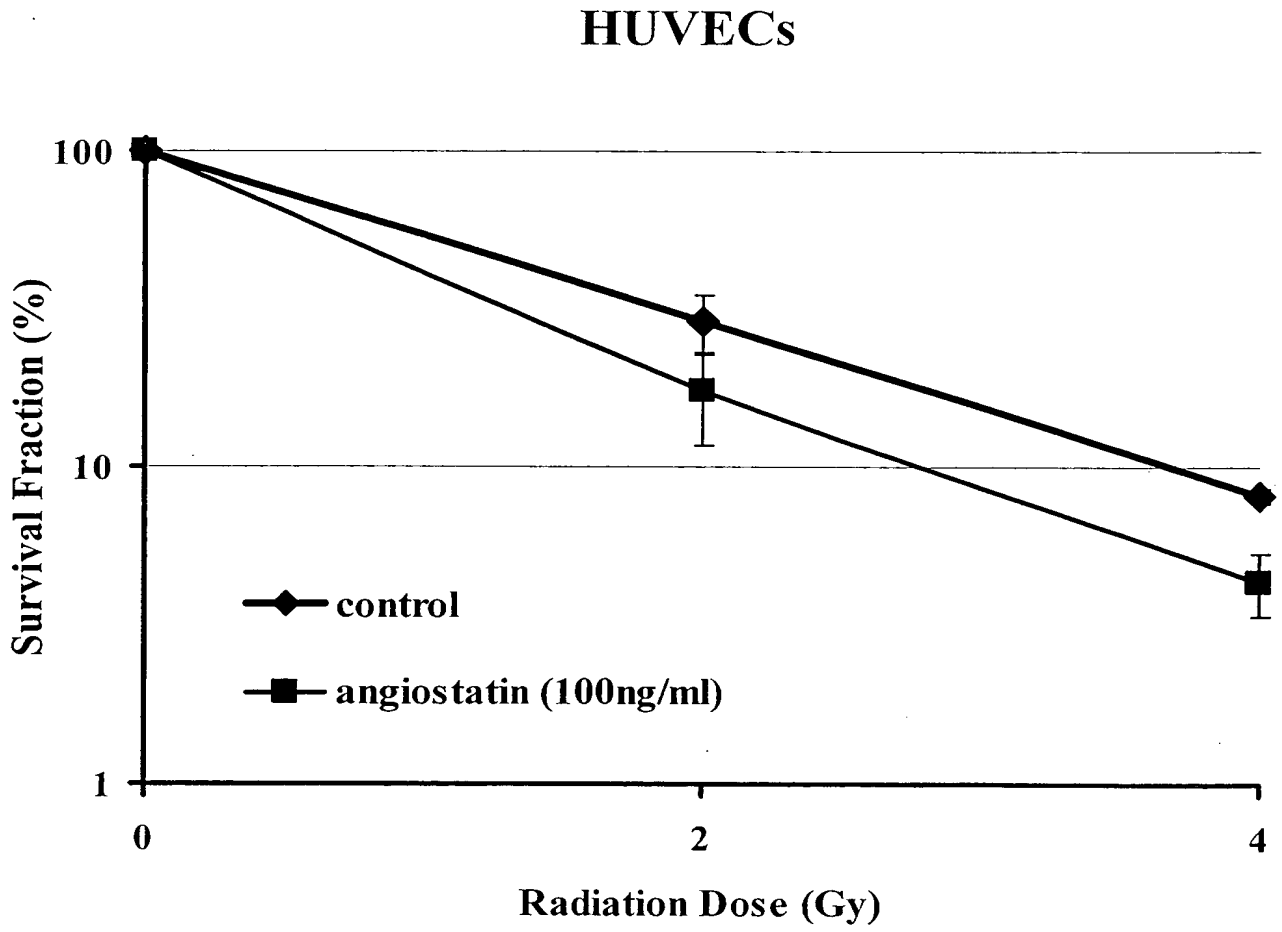

HUVECs
100
10
1
Survival Fraction (%)
control
angiostatin (100ng/ml)
0
2
4
Radiation Dose (Gy)

FIG.59B

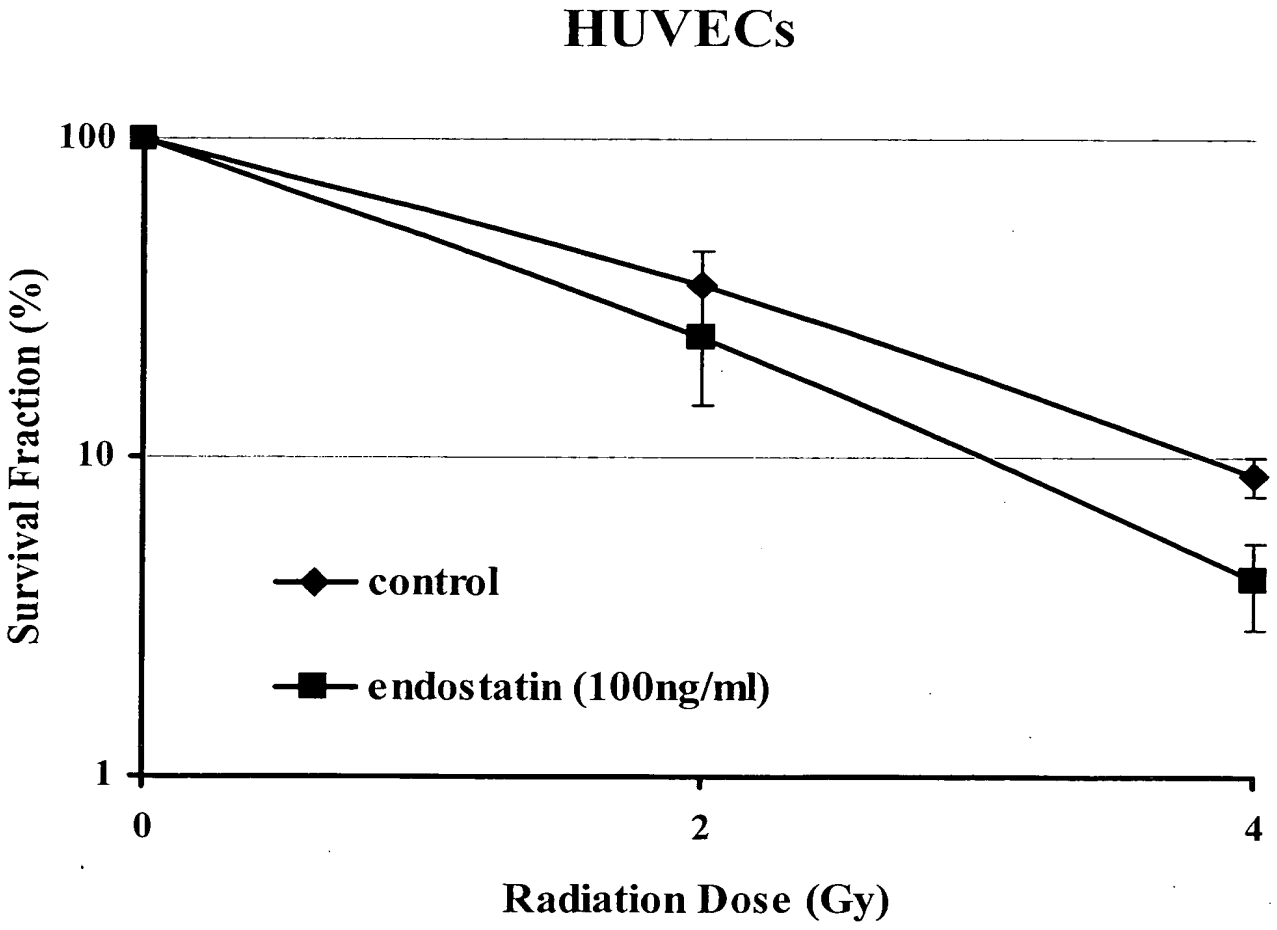

HUVECs
100
10
1
Survival Fraction (%)
control
endostatin (100ng/ml)
0
2
4
Radiation Dose (Gy)

FIG.59C

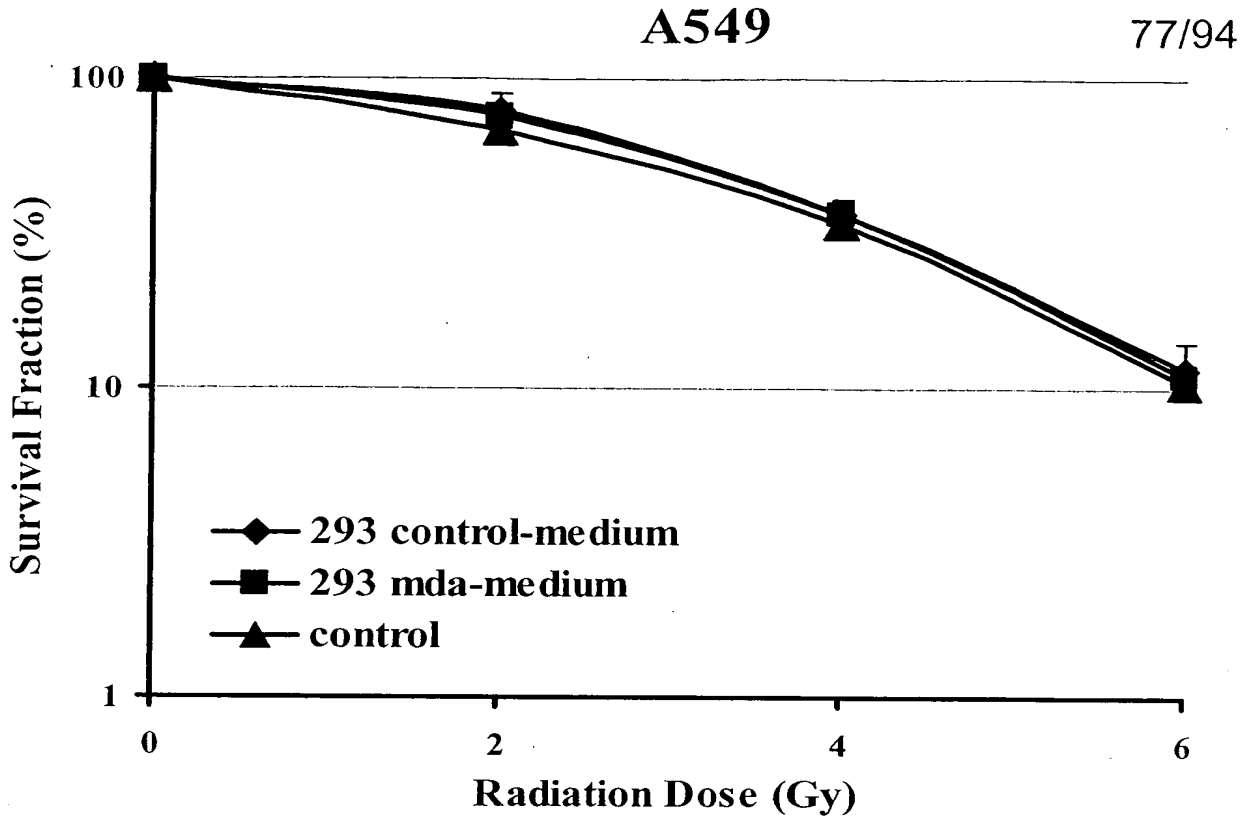


FIG.60A

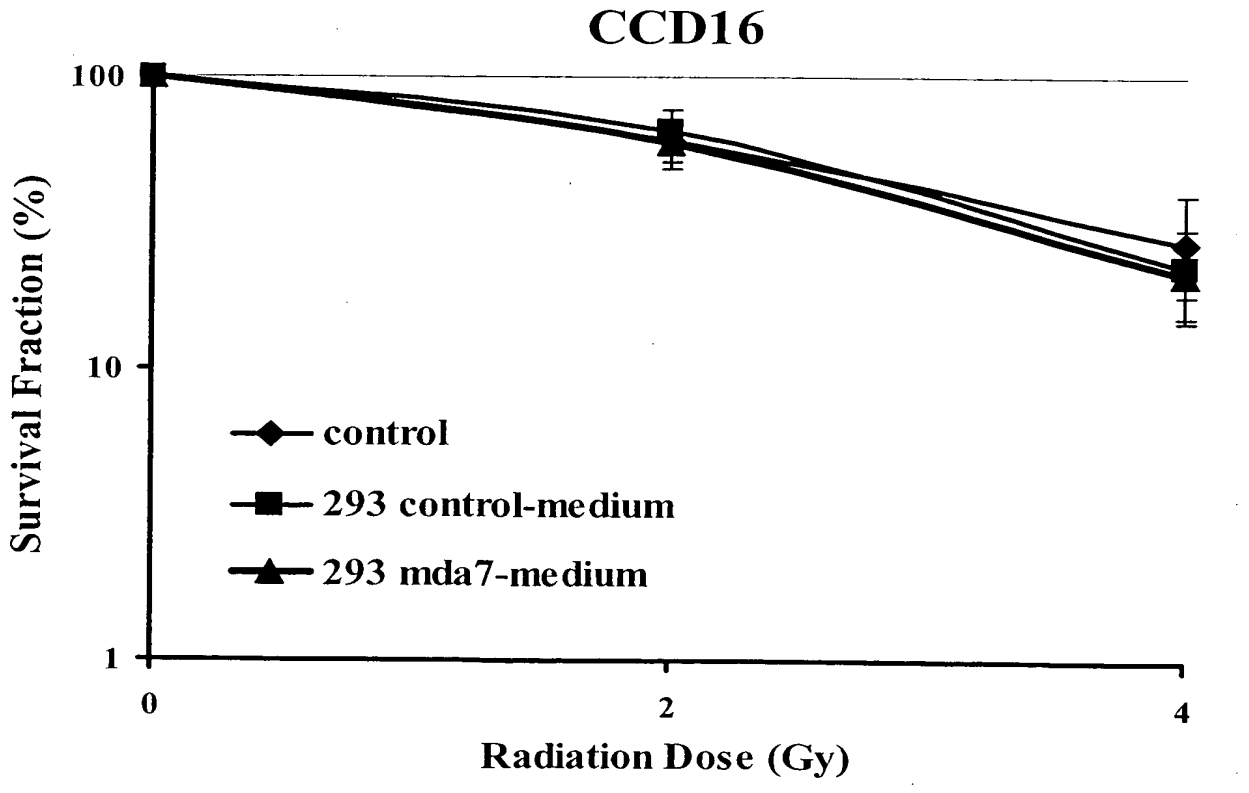


FIG.60B

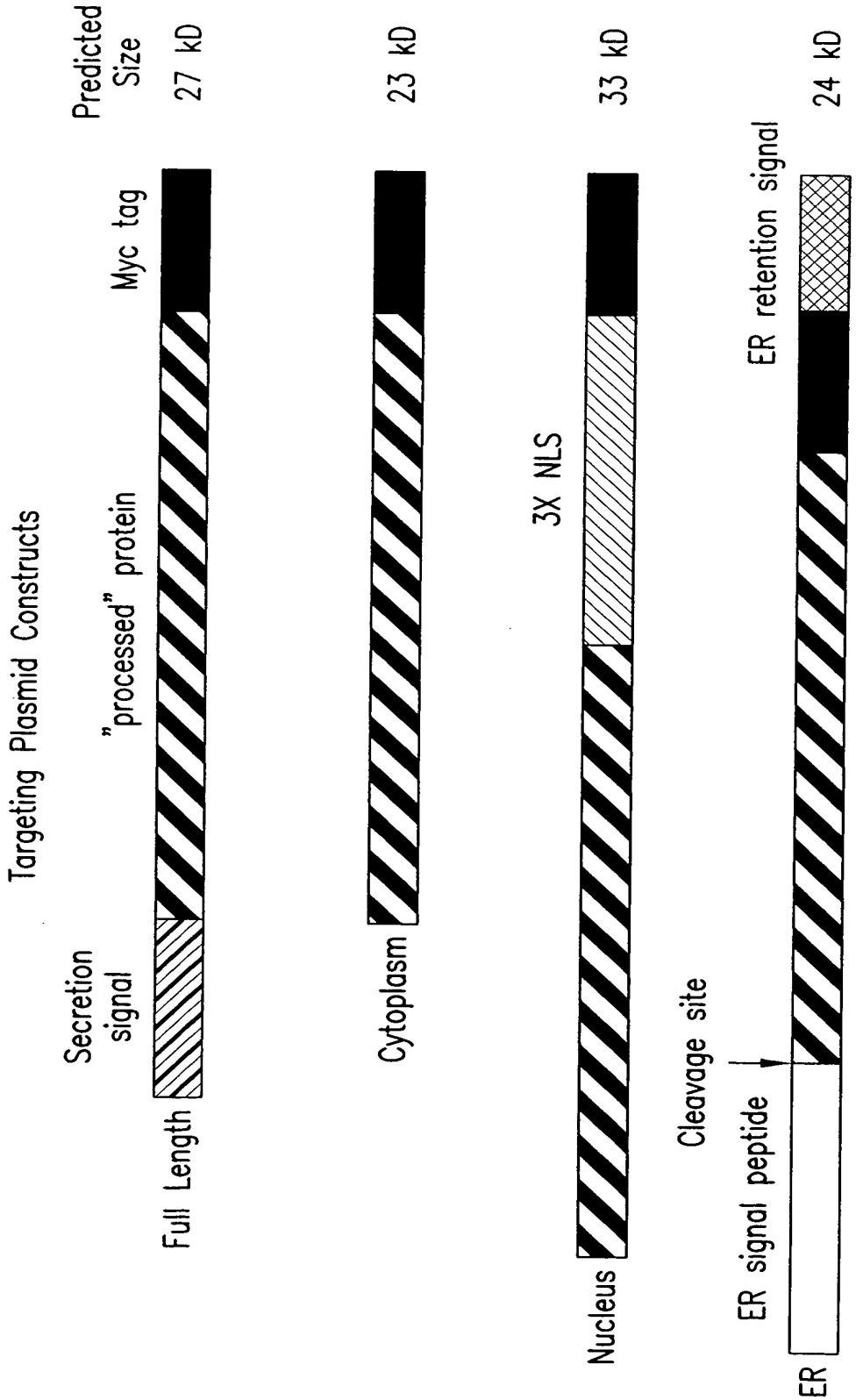

Targeting Plasmid Constructs
Predicted Size
Secretion signal
"processed" protein
Myc tag
27 kD
Full Length
23 kD
Cytoplasm
3X NLS
33 kD
Nucleus
Cleavage site
ER retention signal
24 kD
ER signal peptide
ER

FIG.61

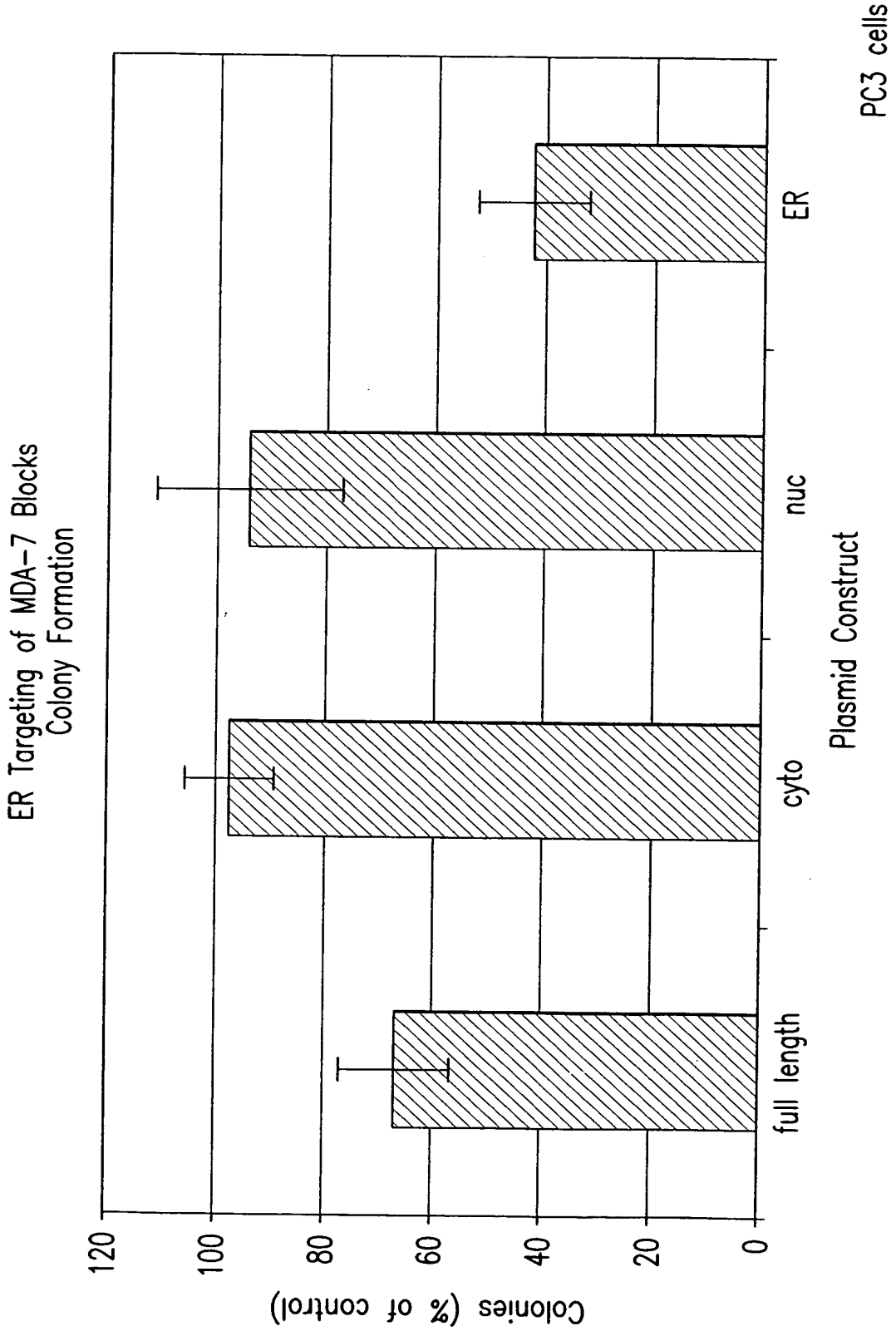

ER Targeting of MDA-7 Blocks
Colony Formation
PC3 cells
Colonies (% of control)
120
100
80
60
40
20
0
full length
cyto
nuc
ER
Plasmid Construct

FIG.62

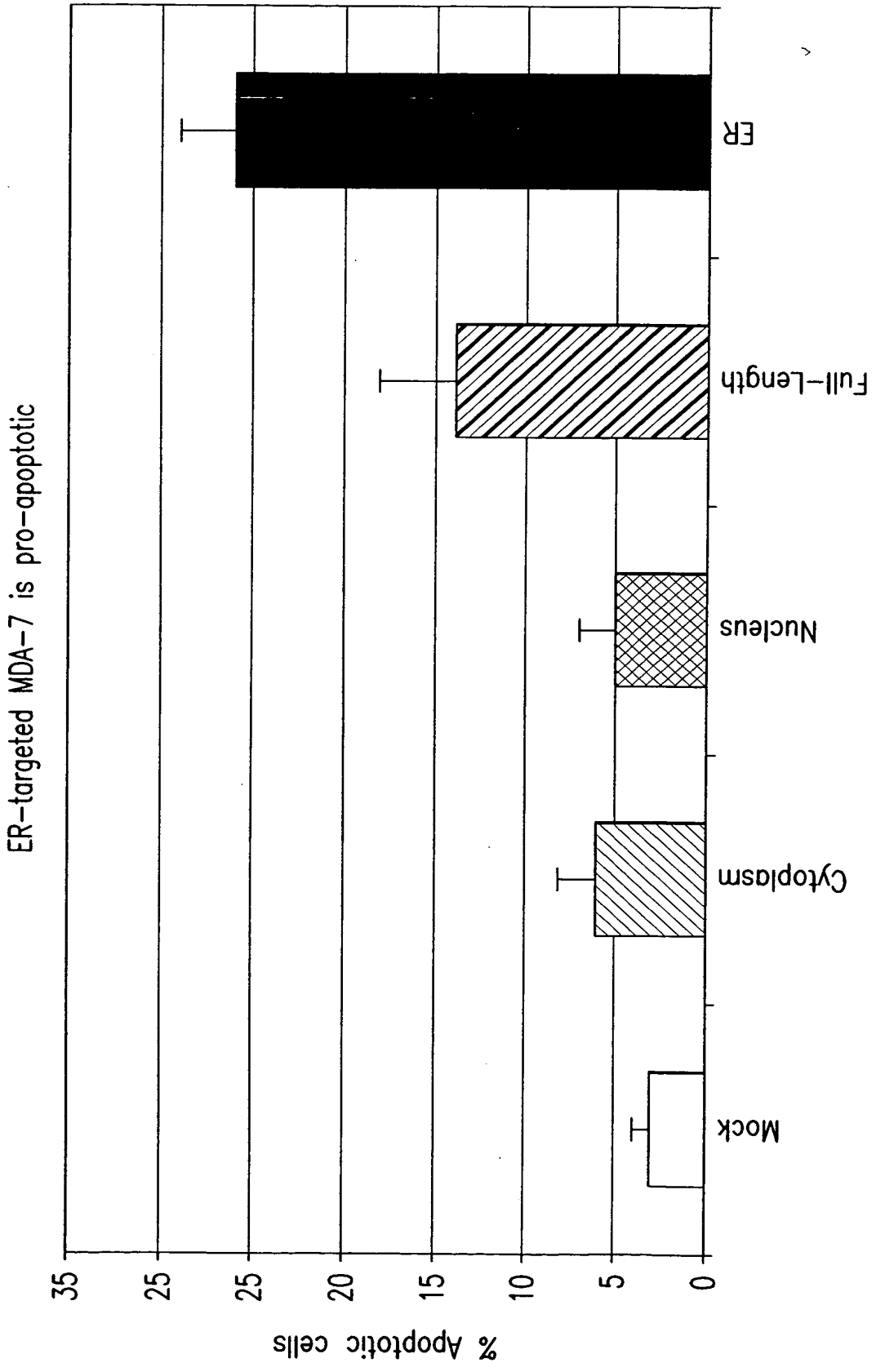

ER-targeted MDA-7 is pro-apoptotic
% Apoptotic cells
35
25
25
20
15
10
5
0
ER
Full-Length
Nucleus
Cytoplasm
Mock

FIG.63

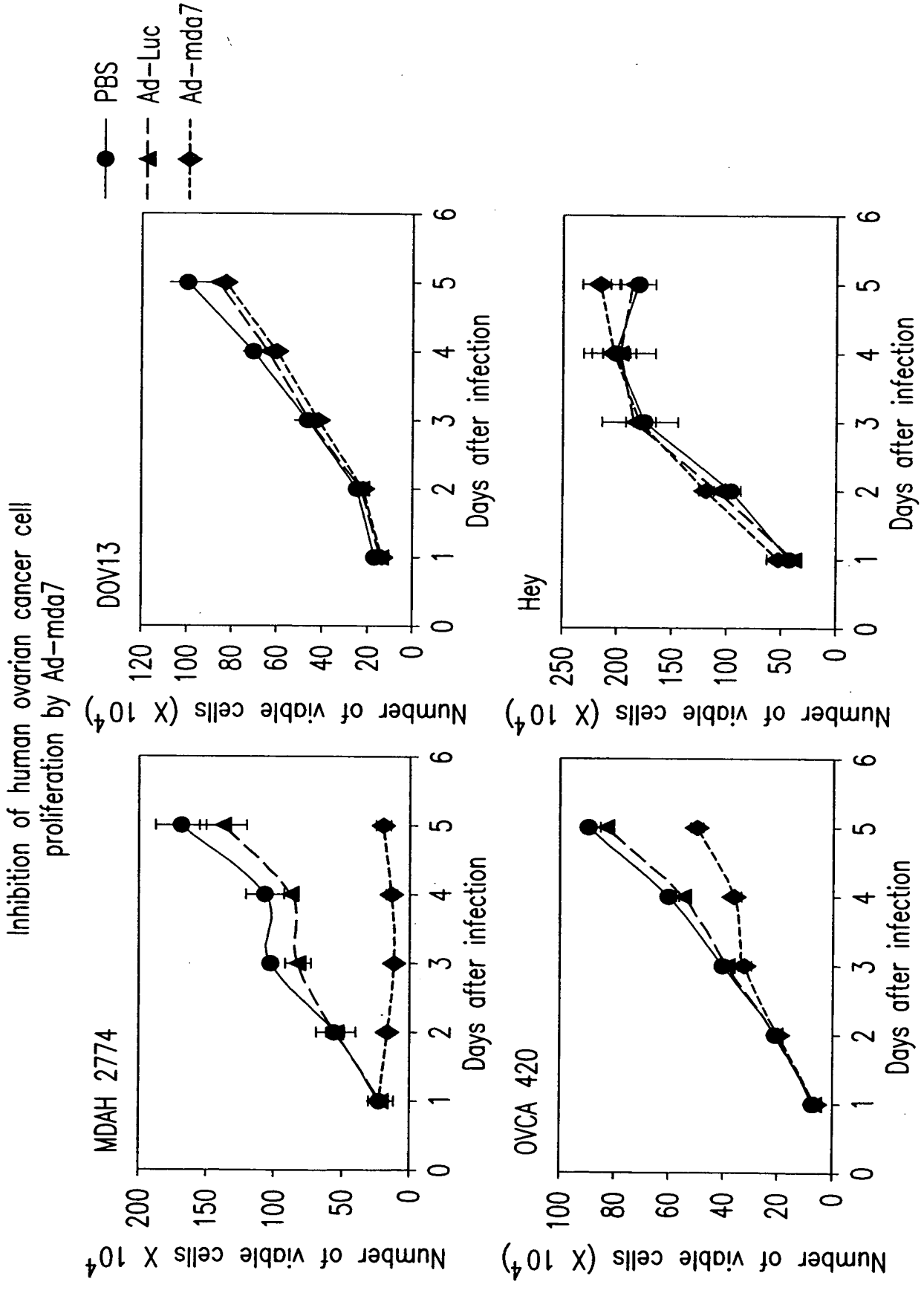

Inhibition of human ovarian cancer cell proliferation by Ad-mda7
PBS
Ad-Luc
Ad-mda7
DOV13
Hey
MDAH 2774
OVCA 420
Number of viable cells (X 10⁴)
Days after infection

FIG.64

Induction of cell cycle arrest by MDA-7
(MDAH 2774)

	G1	S	G2M	Apoptosis Sub G0
24 hrs				
PBS	30.55	34.55	34.9	2.05
Ad.Luc	32.95	36.6	30.45	1.41
Ad.mda-7	27.45	29.75	42.85	4
48 hrs				
PBS	40.8	32.6	26.6	0.955
Ad.Luc	28.75	32.45	38.8	0.84
Ad.mda-7	18.3	78	54.5	10.36

FIG.65A

Replacement Sheet

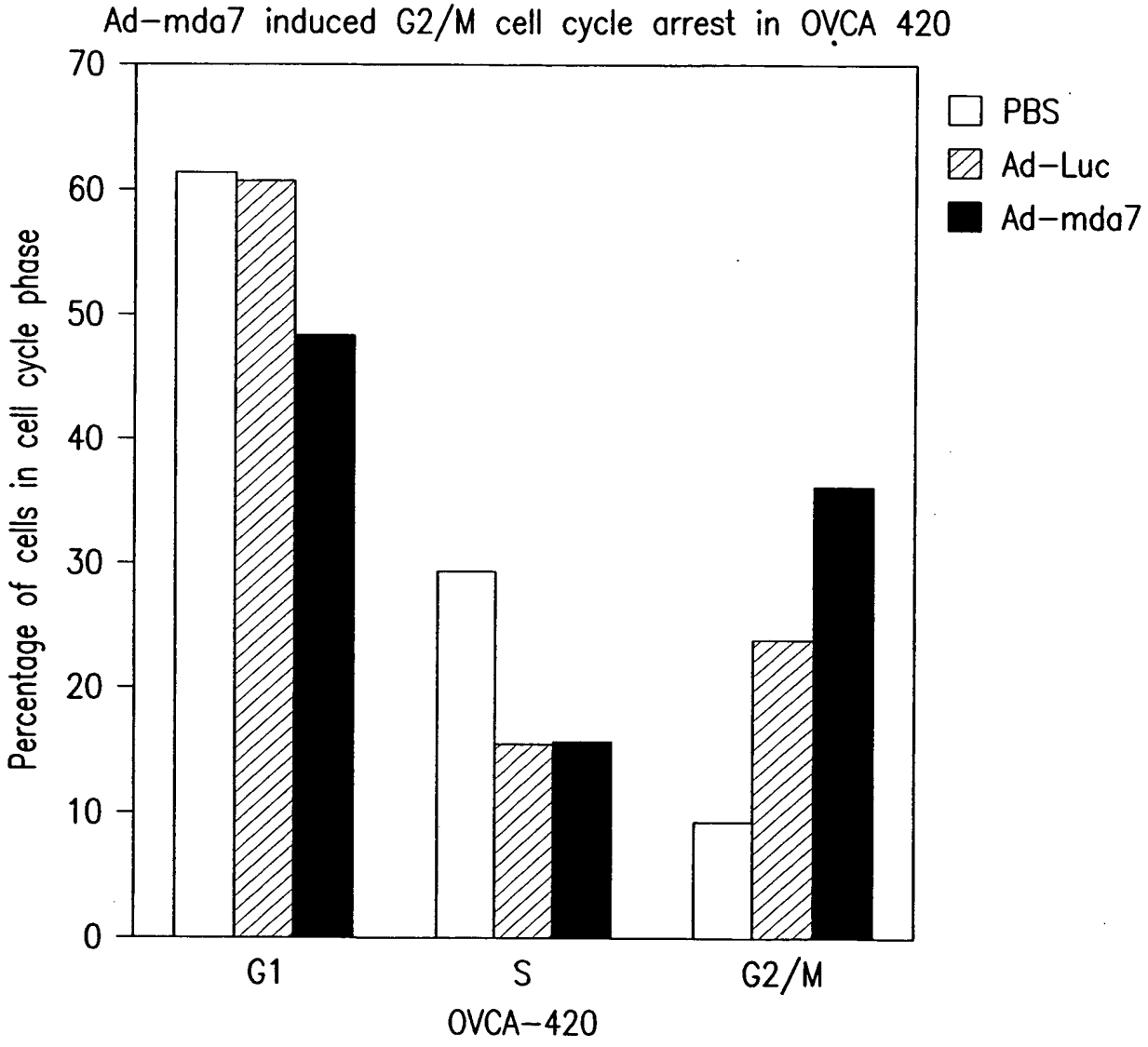

Ad-mda7 induced G2/M cell cycle arrest in OVCA 420
Percentage of cells in cell cycle phase
70
60
50
40
30
20
10
0
G1
S
G2/M
OVCA-420
PBS
Ad-Luc
Ad-mda7

FIG.65B

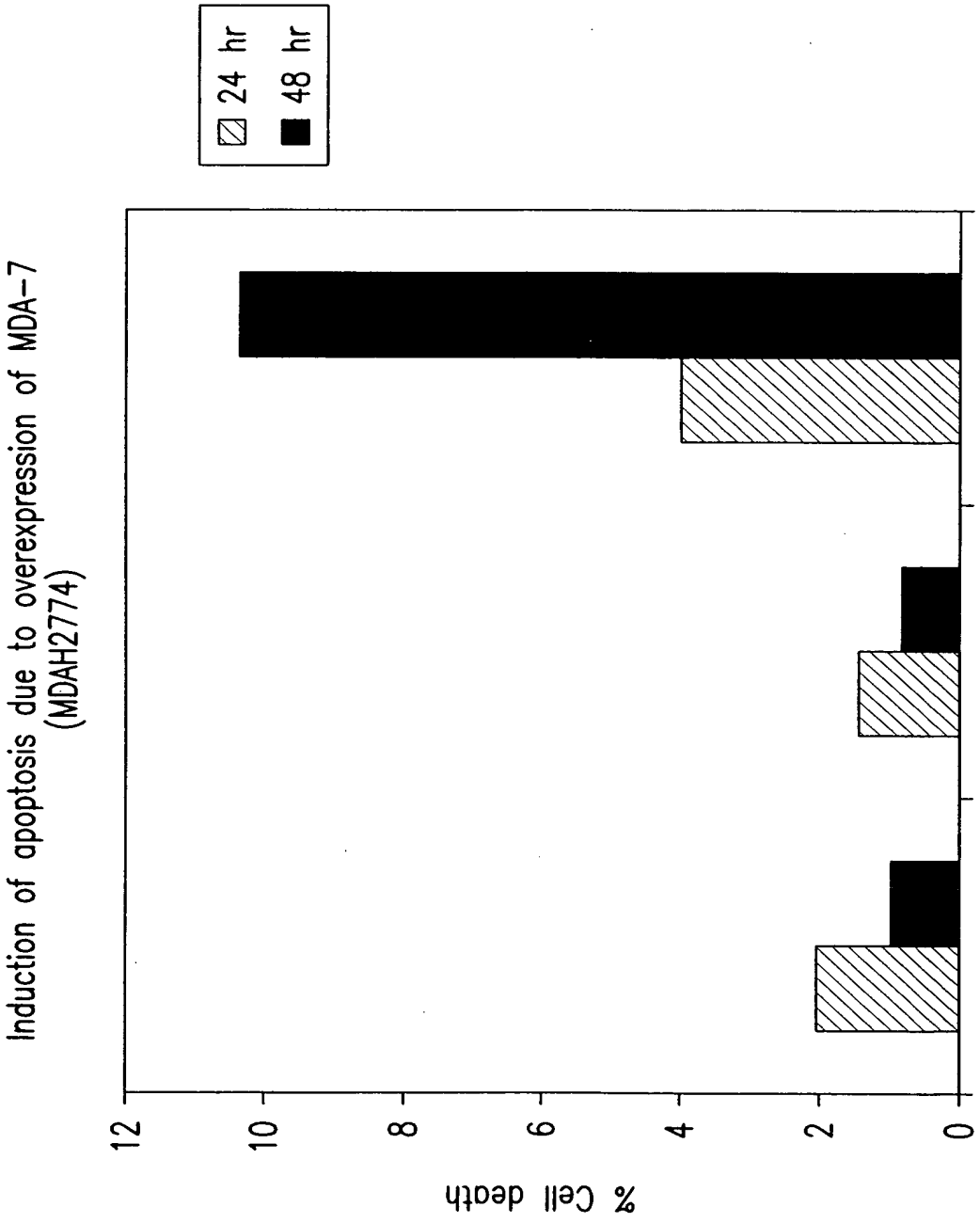

Induction of apoptosis due to overexpression of MDA-7
(MDAH2774)
24 hr
48 hr
% Cell death
0
2
4
6
8
10
12
PBS
Ad.Luc
Ad.Mda-7

FIG.66

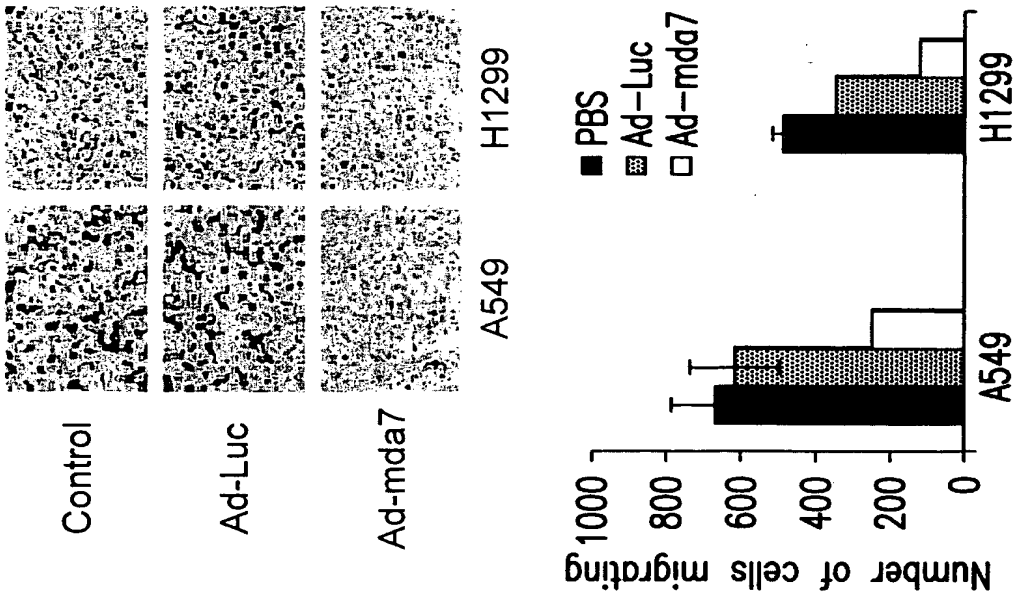


FIG.67A

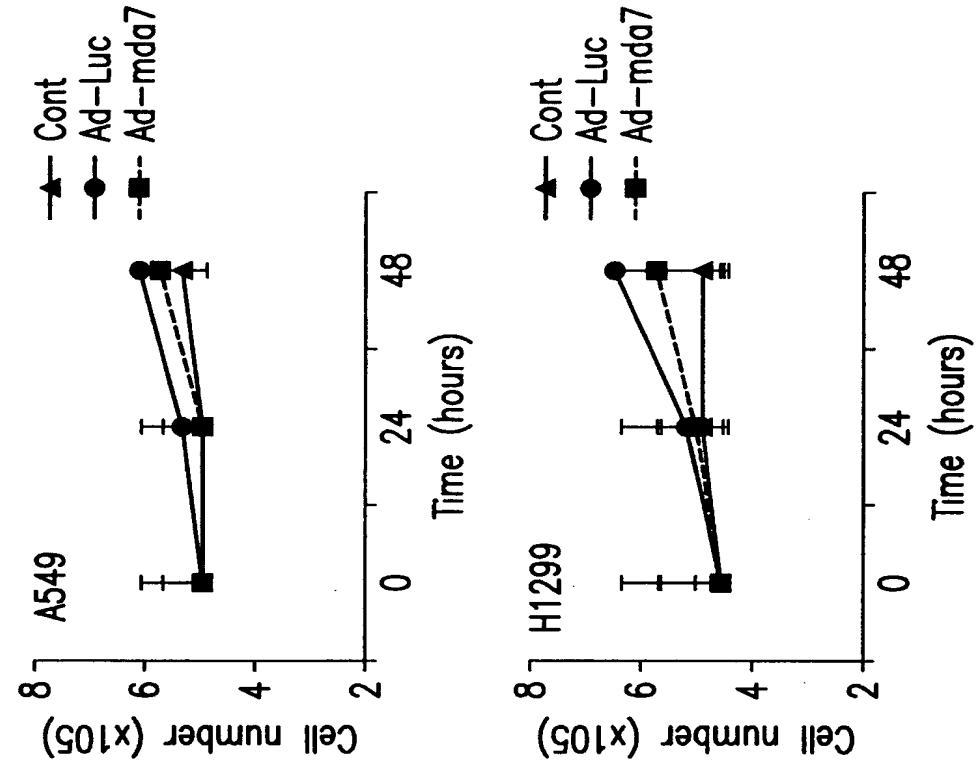


FIG.67B

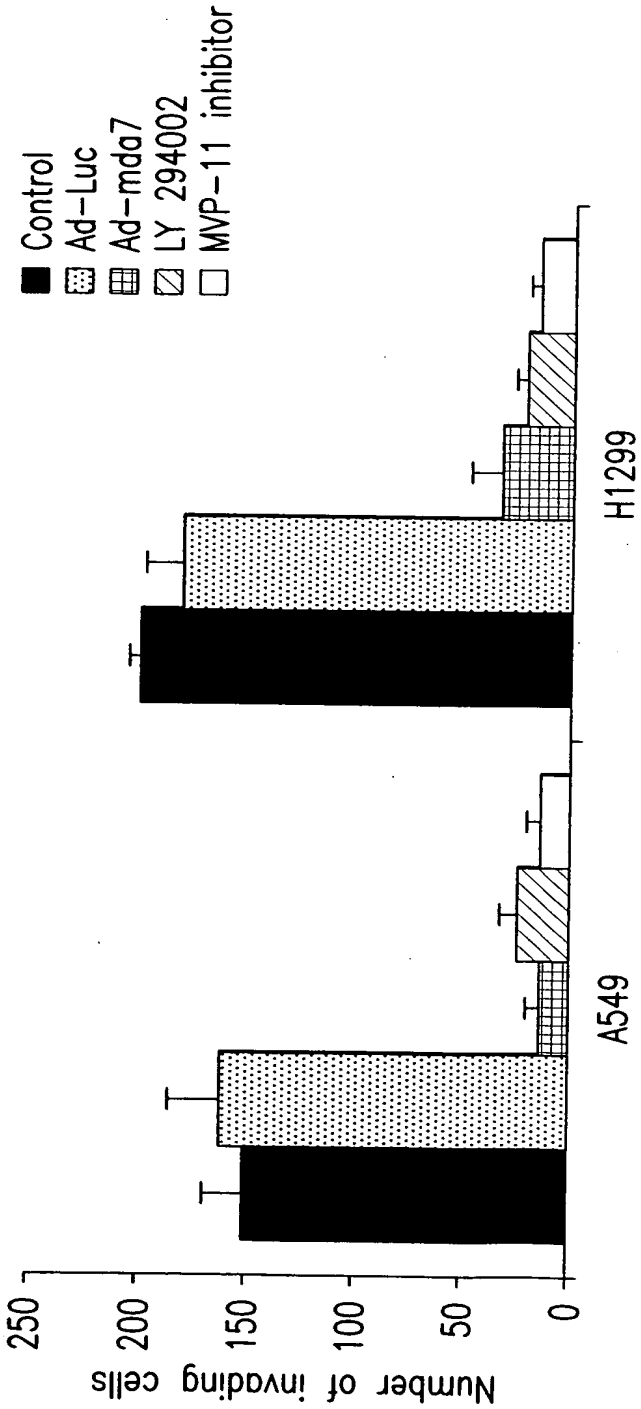

Control
Ad-Luc
Ad-mda7
LY 294002
MVP-11 inhibitor
Number of invading cells
250
200
150
100
50
0
A549
H1299

FIG.68

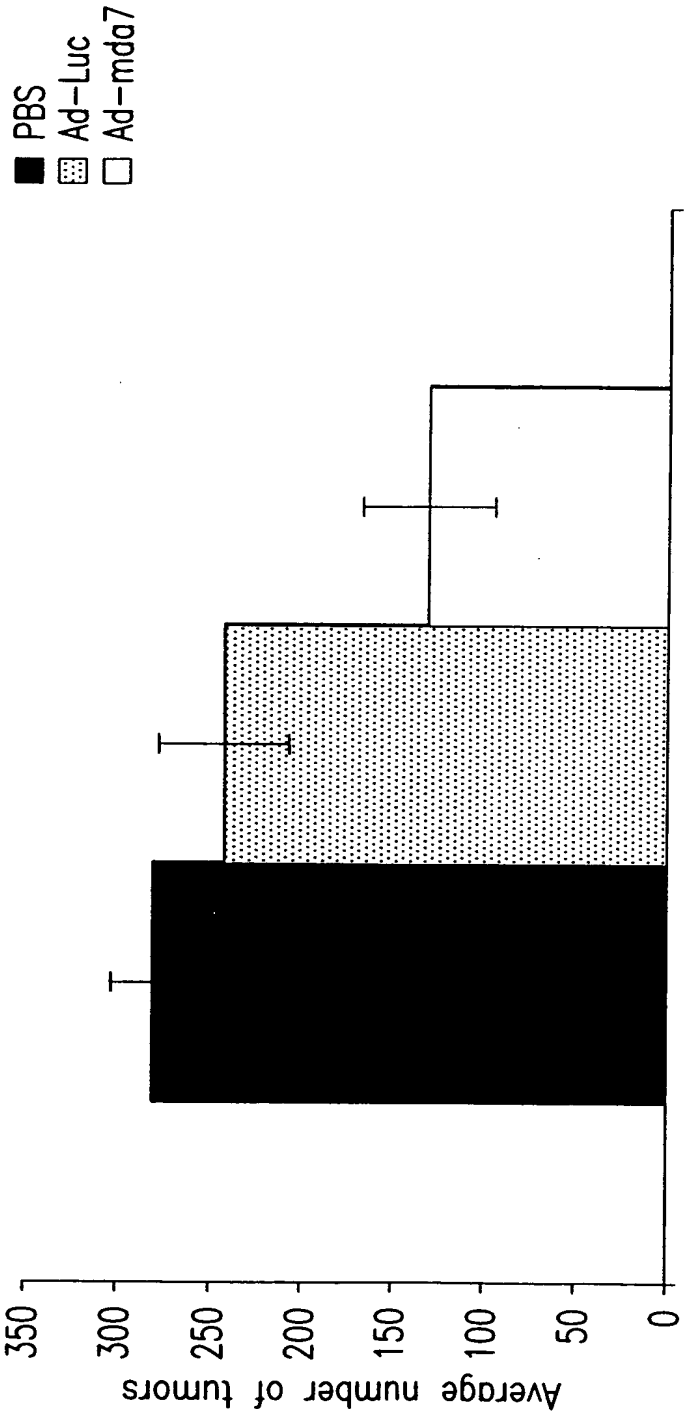

PBS
Ad-Luc
Ad-mda7
Average number of tumors
350
300
250
200
150
100
50
0
Samples

FIG.69

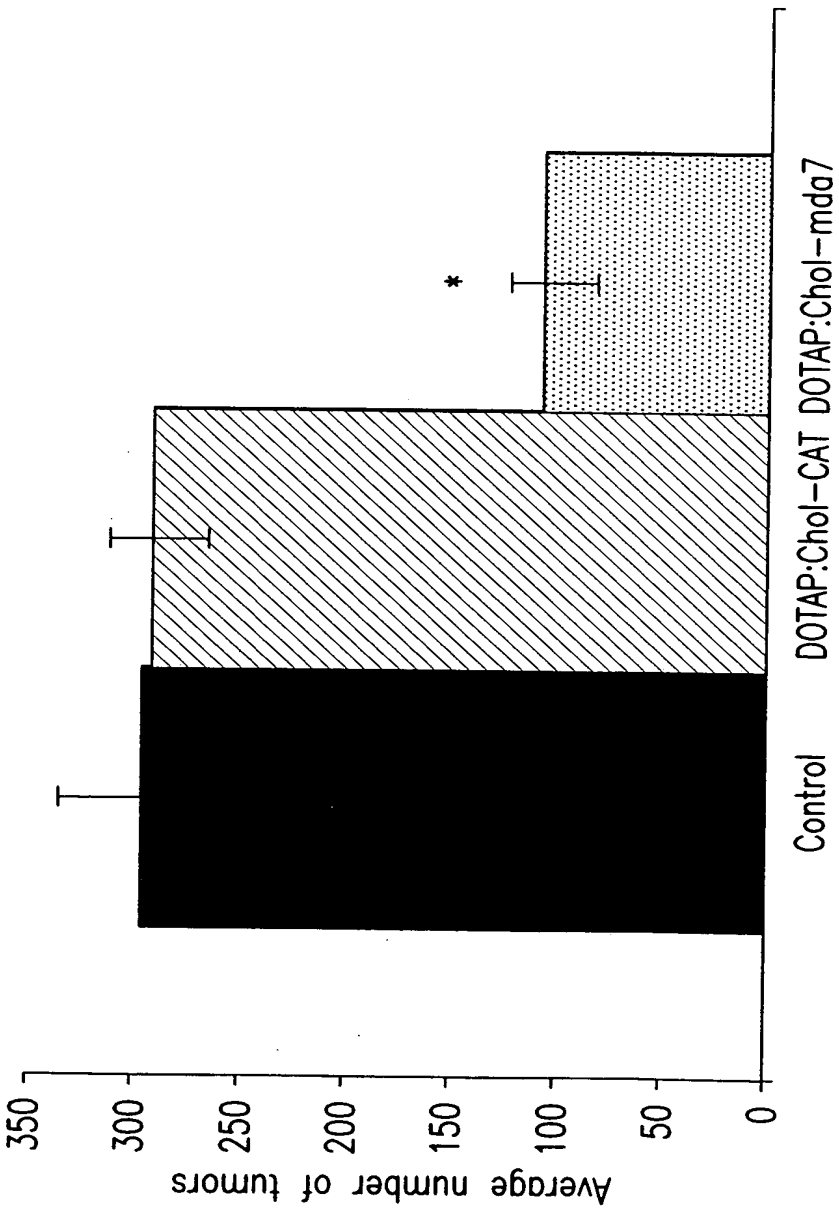

Average number of tumors
350
300
250
200
150
100
50
0
*
Control
DOTAP:Chol-CAT
DOTAP:Chol-mda7

FIG. 70

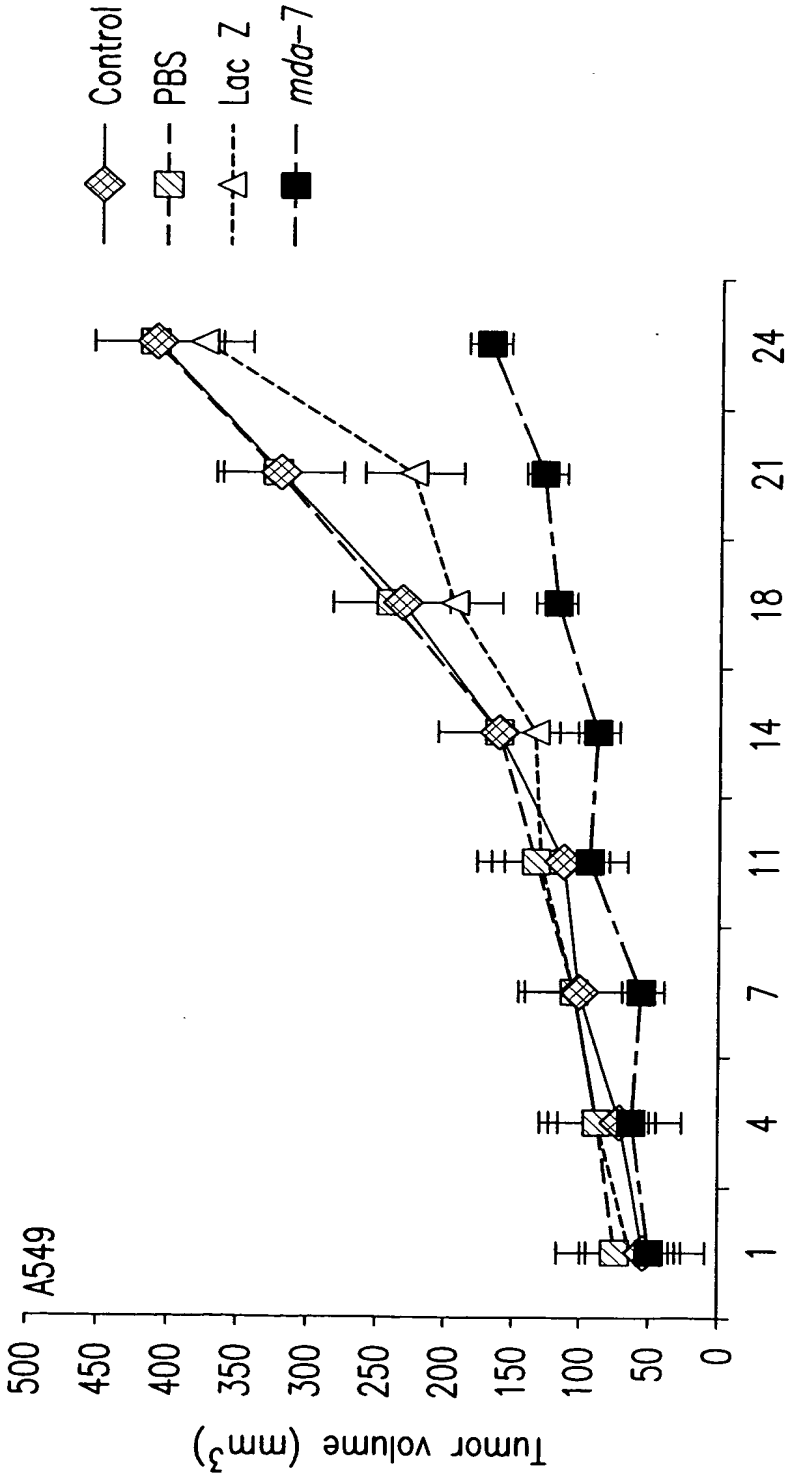

Control
PBS
Lac Z
mda-7
A549
Tumor volume (mm³)
500
450
400
350
300
250
200
150
100
50
0
1
4
7
11
14
18
21
24
Treatment
Time (days)

FIG.71A

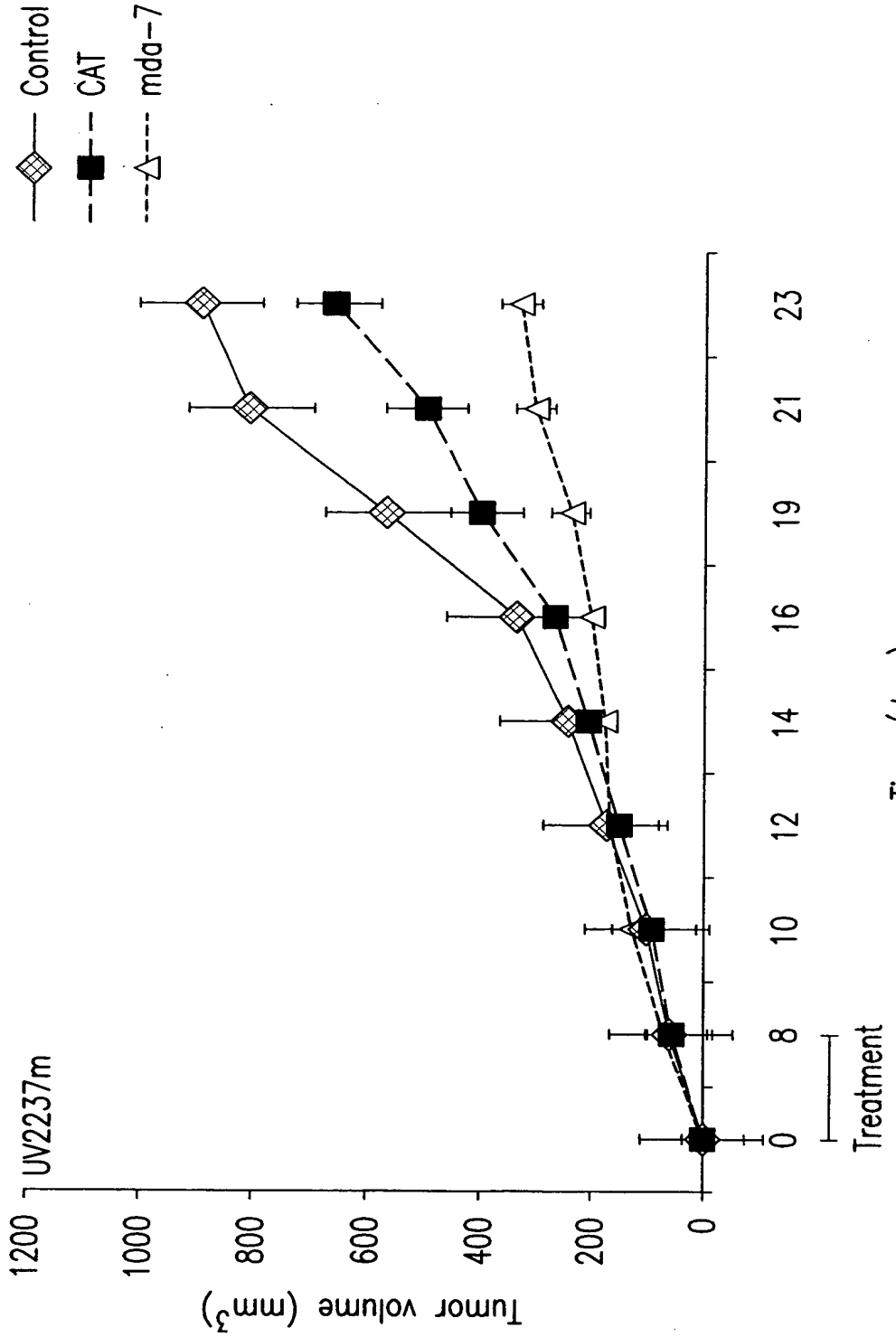

Control
CAT
mda-7
UV2237m
Tumor volume (mm³)
1200
1000
800
600
400
200
0
0
8
10
12
14
16
19
21
23
Time (days)
Treatment

FIG.71B

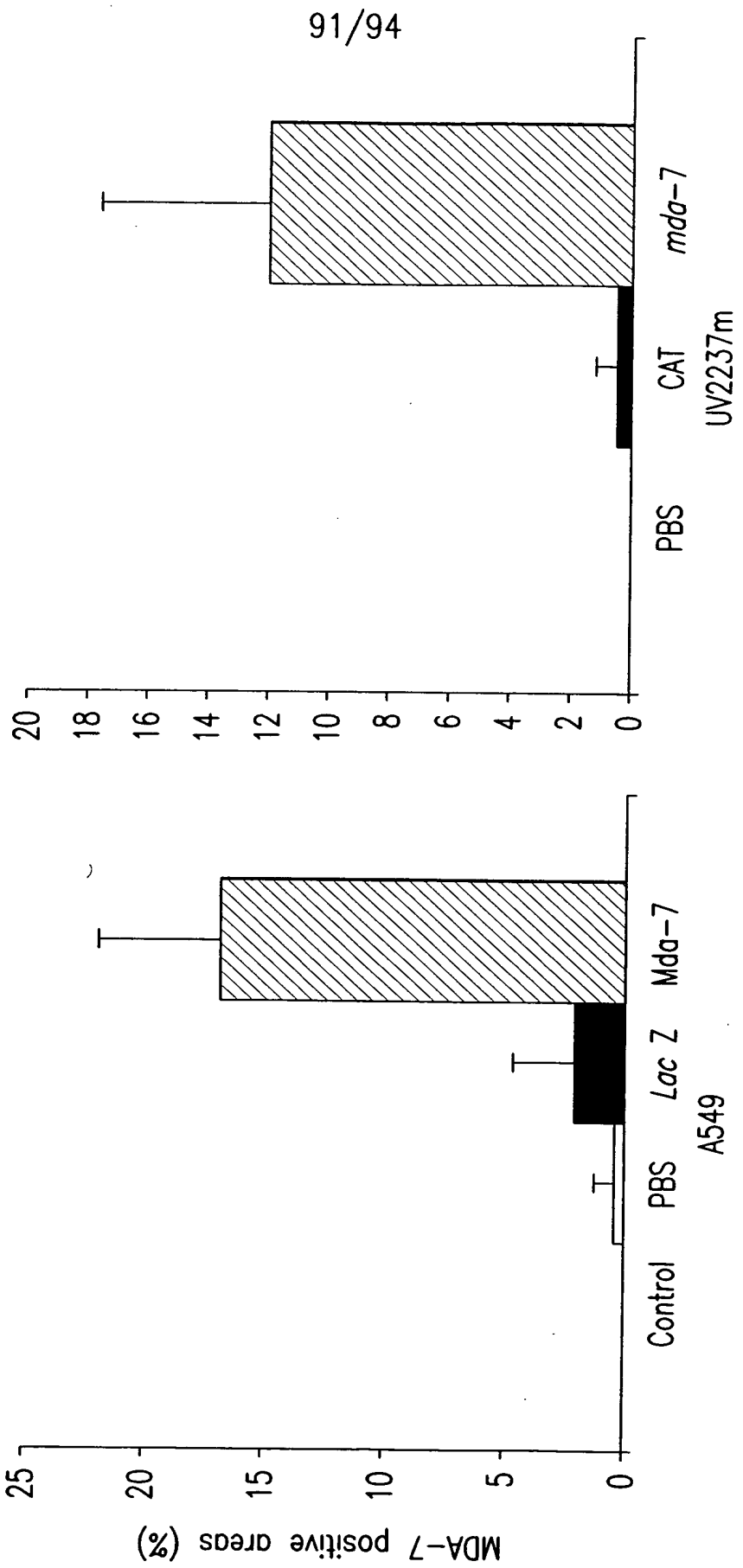

MDA-7 positive areas (%)
0
5
10
15
20
25
Control
PBS
Lac Z
Mda-7
A549
PBS
CAT
UV2237m
mda-7
0
2
4
6
8
10
12
14
16
18
20

FIG. 71C

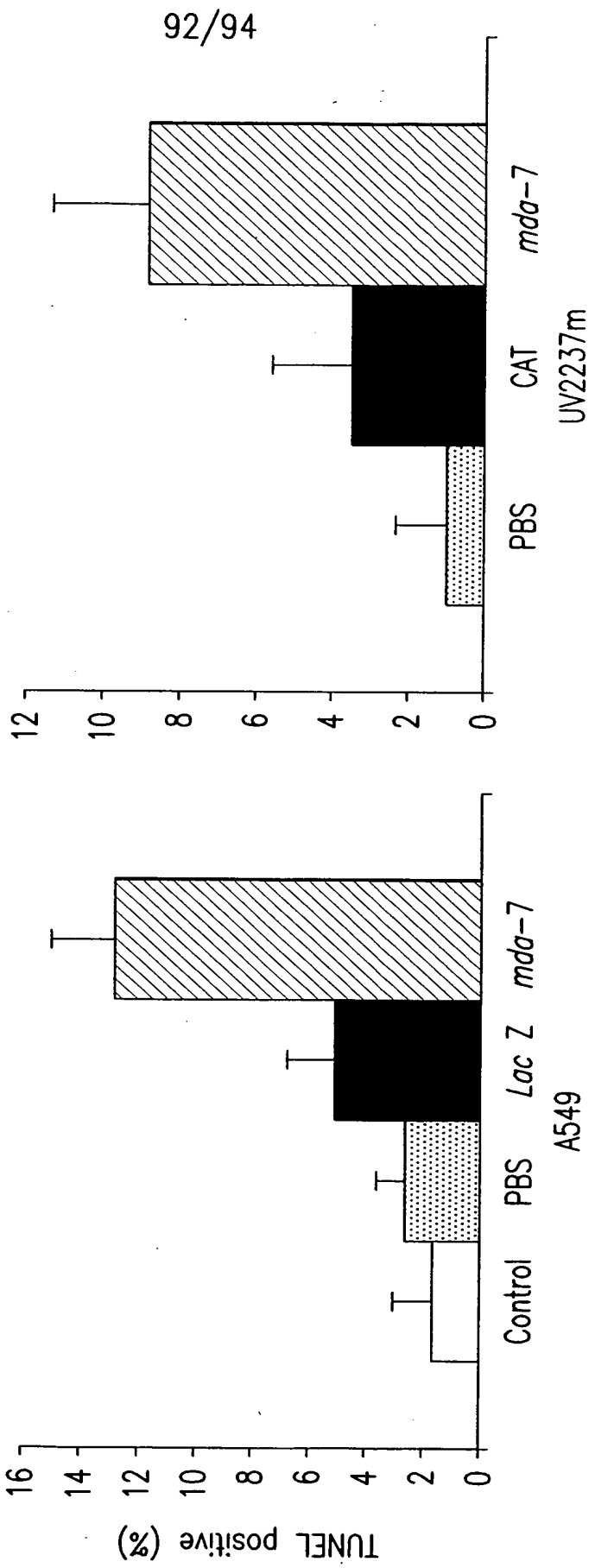

TUNEL positive (%)
0
2
4
6
8
10
12
14
16
Control
PBS
Lac Z
mda-7
A549
0
2
4
6
8
10
12
PBS
CAT
UV2237m
mda-7

FIG.72

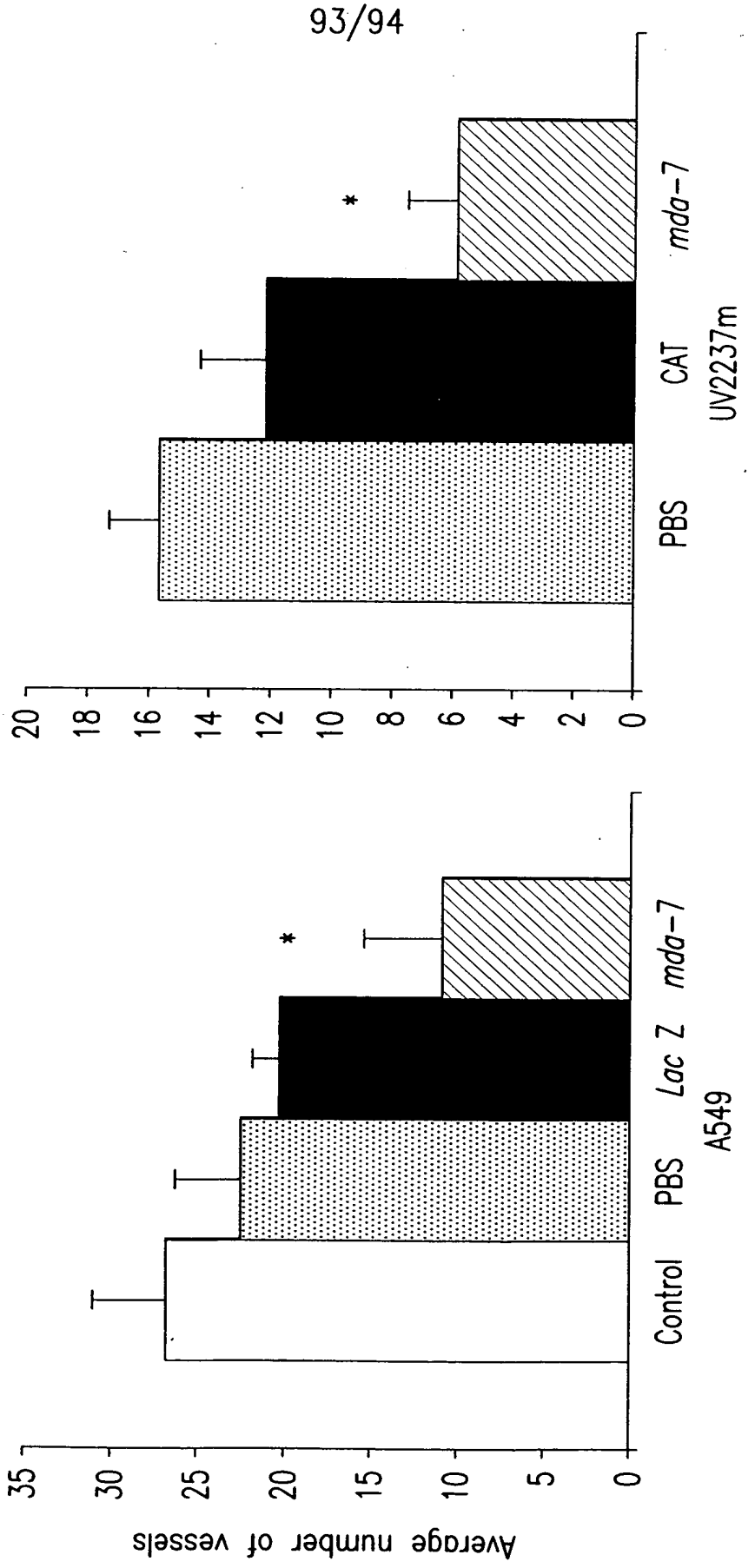

Average number of vessels
0
5
10
15
20
25
30
35
Control
PBS
Lac Z
mda-7
A549
*
0
2
4
6
8
10
12
14
16
18
20
PBS
CAT
UV2237m
mda-7
*

FIG. 73

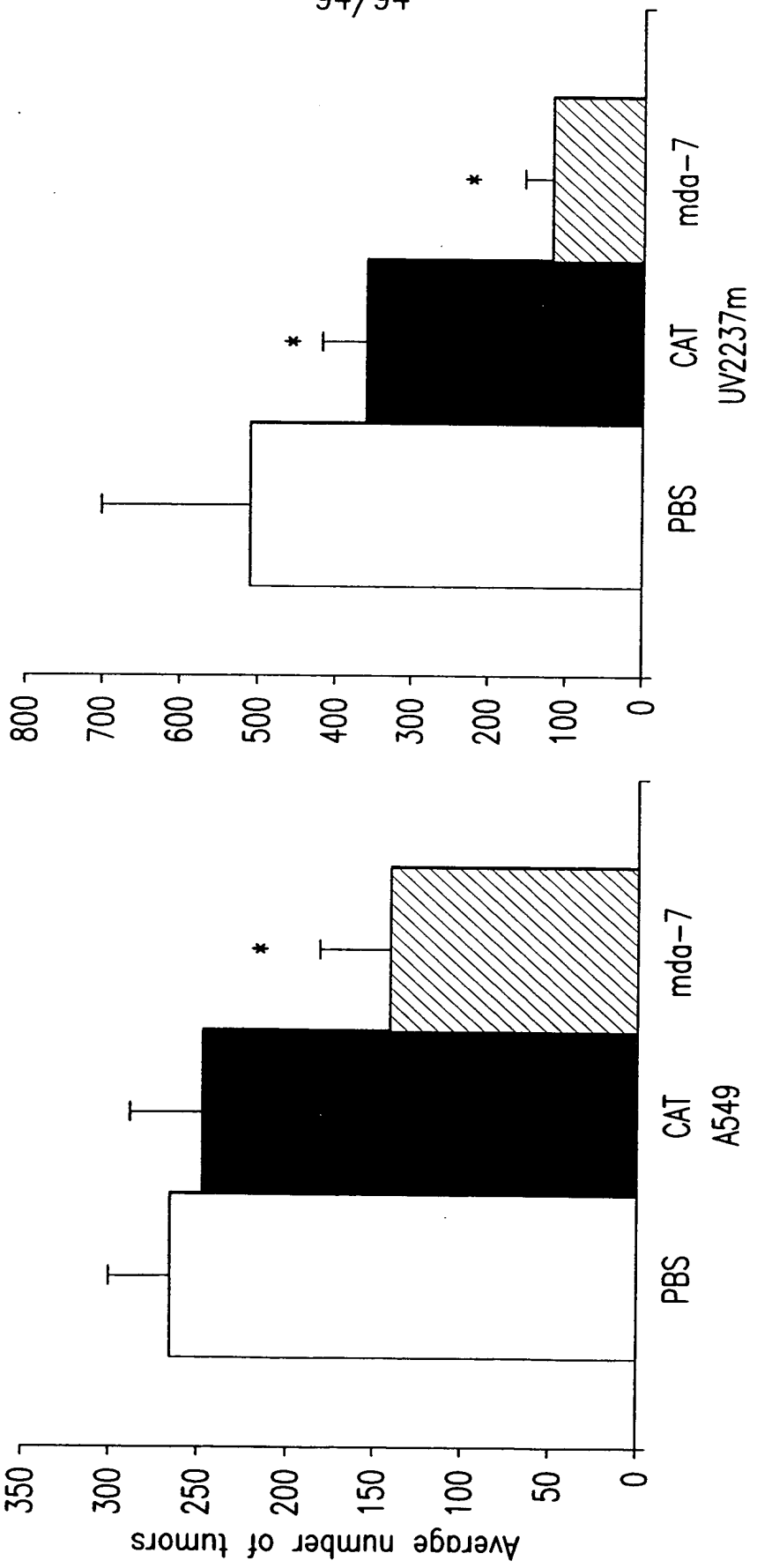

Average number of tumors
0
50
100
150
200
250
300
350
PBS
CAT
mda-7
A549
*
0
100
200
300
400
500
600
700
800
PBS
CAT
mda-7
UV2237m
*
*

FIG. 74

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